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(54) Title: CRYSTALLIZED GLUCOCORTICOID RECEPTOR LIGAND BINDING DOMAIN POLYPEPTIDE AND SCREENING METHODS EMPLOYING SAME

(57) Abstract: A method of modifying a test NR polypeptide is disclosed. The method can include: providing a test NR polypeptide sequence having a characteristic that is targeted for modification; aligning the test NR polypeptide sequence with at least one reference NR polypeptide sequence for which an X-ray structure is available, wherein the at least one reference NR polypeptide sequence has a characteristic that is desired for the test NR polypeptide; building a three-dimensional model for the test NR polypeptide using the three-dimensional coordinates of the X-ray structure(s) of the at least one reference polypeptide and its sequence alignment with the test NR polypeptide sequence; examining the three-dimensional model of the test NR polypeptide for differences with the at least one reference polypeptide that are associated with the desired characteristic; and mutating at least one amino acid residue in the test NR polypeptide sequence located at a difference identified above to a residue associated with the desired characteristic, whereby the test NR polypeptide is modified. An isolated GR polypeptide comprising a mutation in a ligand binding domain, wherein the mutation alters the solubility of the ligand binding domain, is also disclosed. An isolated GR polypeptide, or functional portion thereof, having one or more mutations comprising a substitution of a hydrophobic amino acid residue by a hydrophilic amino acid residue is also disclosed. Representative mutations are F602S and F602D substitutions. Expression of the GR polypeptide in E. coli is also provided. A solved three-dimensional crystal structure of a glucocorticoid receptor a ligand binding domain polypeptide is also disclosed, along with a crystalline form of the glucocorticoid receptor a ligand binding domain polypeptide. Methods of designing modulators of the biological activity of glucocorticoid receptor a and other nuclear receptor, steroid receptor and glucocorticoid receptor polypeptides and nuclear receptor, steroid receptor and glucocorticoid receptor ligand binding domain polypeptides are also disclosed.

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CRYSTALLIZED GLUCOCORTICOID RECEPTOR LIGAND BINDING DOMAIN
POLYPEPTIDE AND SCREENING METHODS EMPLOYING SAME

Cross Reference to Related Applications

5 The present patent application is based on and claims priority to U.S. Provisional Application Serial No. 60/305,902, entitled "CRYSTALLIZED GLUCOCORTICOID RECEPTOR LIGAND BINDING DOMAIN POLYPEPTIDE AND SCREENING METHODS EMPLOYING SAME", which was filed July 17, 2001 and is incorporated herein by reference in its entirety.

10

Technical Field

The present invention relates generally to a modified glucocorticoid receptor polypeptide, to a modified glucocorticoid receptor ligand binding domain polypeptide, to the structure of a glucocorticoid receptor ligand binding domain, and to the structure of a glucocorticoid receptor ligand binding domain in complex with a ligand and a co-activator. The invention further relates to methods by which a soluble glucocorticoid polypeptide can be generated and by which modulators and ligands of nuclear receptors, particularly steroid receptors and more particularly glucosteroid receptors and the ligand binding domains thereof can be identified.

20

Abbreviations

	ATP	adenosine triphosphate
	ADP	adenosine diphosphate
25	AR	androgen receptor
	CAT	chloramphenicol acyltransferase
	CBP	CREB binding protein
	cDNA	complementary DNA
	DBD	DNA binding domain
30	DMSO	dimethyl sulfoxide
	DNA	deoxyribonucleic acid
	DTT	dithiothreitol
	EDTA	ethylenediaminetetraacetic acid

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	ER	estrogen receptor
	GR	glucocorticoid receptor
	GRE	glucocorticoid responsive element
	GST	glutathione S-transferase
5	HEPES	N-2-Hydroxyethylpiperazine-N'-2-ethanesulfonic acid
	HSP	heat shock protein
	kDa	kilodalton(s)
	LBD	ligand binding domain
	MR	mineralcorticoid receptor
10	NDP	nucleotide diphosphate
	NID	nuclear receptor interaction domain
	NTP	nucleotide triphosphate
	PAGE	polyacrylamide gel electrophoresis
	PCR	polymerase chain reaction
15	pI	isoelectric point
	PPAR	peroxisome proliferator-activated receptor
	PR	progesterone receptor
	RAR	retinoid acid receptor
	RXR	retinoid X receptor
20	SDS	sodium dodecyl sulfate
	SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel electrophoresis
	TIF2	transcription intermediary factor 2
	TR	thyroid receptor
25	VDR	vitamin D receptor

Amino Acid Abbreviations

	<u>Single-Letter Code</u>	<u>Three-Letter Code</u>	<u>Name</u>
	A	Ala	Alanine
30	V	Val	Valine
	L	Leu	Leucine
	I	Ile	Isoleucine
	P	Pro	Proline

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	F	Phe	Phenylalanine
	W	Trp	Tryptophan
	M	Met	Methionine
5	G	Gly	Glycine
	S	Ser	Serine
	T	Thr	Threonine
	C	Cys	Cysteine
	Y	Tyr	Tyrosine
10	N	Asn	Asparagine
	Q	Gln	Glutamine
	D	Asp	Aspartic Acid
	E	Glu	Glutamic Acid
	K	Lys	Lysine
15	R	Arg	Arginine
	H	His	Histidine

Functionally Equivalent Codons

	<u>Amino Acid</u>		<u>Codons</u>
20	Alanine	Ala	A GCA GCC GCG GCU
	Cysteine	Cys	C UGC UGU
	Aspartic Acid	Asp	D GAC GAU
	Glumatic acid	Glu	E GAA GAG
	Phenylalanine	Phe	F UUC UUU
	Glycine	Gly	G GGA GGC GGG GGU
25	Histidine	His	H CAC CAU
	Isoleucine	Ile	I AUA AUC AUU
	Lysine	Lys	K AAA AAG
	Methionine	Met	M AUG
	Asparagine	Asn	N AAC AAU
30	Proline	Pro	P CCA CCC CCG CCU
	Glutamine	Gln	Q CAA CAG
	Threonine	Thr	T ACA ACC ACG ACU
	Valine	Val	V GUA GUC GUG GUU

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	Tryptophan	Trp	W	UGG
	Tyrosine	Tyr	Y	UAC UAU
	Leucine	Leu	L	UUA UUG CUA CUC CUG CUU
5	Arginine	Arg	R	AGA AGG CGA CGC CGG CGU
	Serine	Ser	S	ACG AGU UCA UCC UCG UCU

10

Background Art

Nuclear receptors reside in either the cytoplasm or nucleus of eukaryotic cells and represent a superfamily of proteins that specifically bind a physiologically relevant small molecule, such as a hormone or vitamin. As a result of a molecule binding to a nuclear receptor, the nuclear receptor changes the ability of a cell to transcribe DNA, i.e. nuclear receptors modulate the transcription of DNA. However, they can also have transcription independent actions.

Unlike integral membrane receptors and membrane-associated receptors, nuclear receptors reside in either the cytoplasm or nucleus of eukaryotic cells. Thus, nuclear receptors comprise a class of intracellular, soluble, ligand-regulated transcription factors. Nuclear receptors include but are not limited to receptors for androgens, mineralcorticoids, progestins, estrogens, thyroid hormones, vitamin D, retinoids, eicosanoids, peroxisome proliferators and, pertinently, glucocorticoids. Many nuclear receptors, identified by either sequence homology to known receptors (See, e.g., Drewes et al., (1996) *Mol. Cell. Biol.* 16:925-31) or based on their affinity for specific DNA binding sites in gene promoters (See, e.g., Sladek et al., *Genes Dev.* 4:2353-65), have unascertained ligands and are therefore commonly termed "orphan receptors".

Glucocorticoids are an example of a cellular molecule that has been associated with cellular proliferation. Glucocorticoids are known to induce growth arrest in the G1-phase of the cell cycle in a variety of cells, both *in vivo* and *in vitro*, and have been shown to be useful in the treatment of certain cancers. The glucocorticoid receptor (GR) belongs to an important class of transcription factors that alter the expression of target genes in response to a specific hormone signal.

Accumulated evidence indicates that receptor associated proteins play key roles in regulating glucocorticoid signaling. The list of cellular proteins that can bind and co-purify with the GR is constantly expanding.

Glucocorticoids are also used for their anti-inflammatory effect on the skin, joints, and tendons. They are important for treatment of disorders where inflammation is thought to be caused by immune system activity. Representative disorders of this sort include but are not limited to rheumatoid arthritis, inflammatory bowel disease, glomerulonephritis, and connective tissue diseases like systemic lupus erythematosus. Glucocorticoids are also used to treat asthma and are widely used with other drugs to prevent the rejection of organ transplants. Some cancers of the blood (leukemias) and lymphatic system (lymphomas) can also respond to corticosteroid drugs.

Glucocorticoids exert several effects in tissues that express receptors for them. They regulate the expression of several genes either positively or negatively and in a direct or indirect manner. They are also known to arrest the growth of certain lymphoid cells and in some cases cause cell death (Harmon et al., (1979) *J. Cell Physiol.* 98: 267-278; Yamamoto, (1985) *Ann. Rev. Genet.* 19: 209-252; Evans, (1988) *Science* 240:889-895; Beato, (1989) *Cell* 56:335-344; Thompson, (1989) *Cancer Res.* 49: 2259s-2265s.). Due in part to their ability to kill cells, glucocorticoids have been used for decades in the treatment of leukemias, lymphomas, breast cancer, solid tumors and other diseases involving irregular cell growth, e.g. psoriasis. The inclusion of glucocorticoids in chemotherapeutic regimens has contributed to a high rate of cure of certain leukemias and lymphomas which were formerly lethal (Homo-Delarche, (1984) *Cancer Res.* 44: 431-437). Although it is clear that glucocorticoids exert these effects after binding to their receptors, the mechanism of cell kill is not completely understood, although several hypotheses have been proposed. Among the more prominent hypotheses are: the deinduction of critical lymphokines, oncogenes and growth factors; the induction of supposed "lysis genes"; alterations in calcium ion influx; the induction of endonucleases; and the induction of a cyclic AMP-dependent protein kinase (McConkey et al., (1989) *Arch. Biochem. Biophys.* 269: 365-370; Cohen & Duke, (1984) *J. Immunol.* 152: 38-42; Eastman-Reks & Vedeckis, (1986) *Cancer Res.* 46: 2457-2462; Kelso & Munck, (1984) *J. Immunol.*

133:784-791; Gruol et al., (1989) *Molec. Endocrinol.* 3: 2119-2127; Yuh & Thompson, (1989) *J. Biol. Chem.* 264: 10904-10910).

Polypeptides, including the glucocorticoid receptor ligand binding domain, have a three-dimensional structure determined by the primary amino acid sequence and the environment surrounding the polypeptide. This three-dimensional structure establishes the polypeptide's activity, stability, binding affinity, binding specificity, and other biochemical attributes. Thus, knowledge of a protein's three-dimensional structure can provide much guidance in designing agents that mimic, inhibit, or improve its biological activity.

The three-dimensional structure of a polypeptide can be determined in a number of ways. Many of the most precise methods employ X-ray crystallography (See, e.g., Van Holde, (1971) *Physical Biochemistry*, Prentice-Hall, New Jersey, pp. 221-39). This technique relies on the ability of crystalline lattices to diffract X-rays or other forms of radiation. Diffraction experiments suitable for determining the three-dimensional structure of macromolecules typically require high-quality crystals. Unfortunately, such crystals have been unavailable for the ligand binding domain of a human glucocorticoid receptor, as well as many other proteins of interest. Thus, high-quality diffracting crystals of the ligand binding domain of a human glucocorticoid receptor in complex with a ligand and a peptide would greatly assist in the elucidation of its three-dimensional structure.

Clearly, the solved crystal structure of the ligand binding domain of a glucocorticoid receptor polypeptide would be useful in the design of modulators of activity mediated by the glucocorticoid receptor. Evaluation of the available sequence data shows that GR α is particularly similar to MR, PR and AR. The GR α LBD has approximately 56%, 54% and 50% sequence identity to the MR, PR and AR LBDs, respectively. The GR β amino acid sequence is identical to the GR α amino acid sequence for residues 1-727, but the remaining 15 residues in GR β show no significant similarity to the remaining 50 residues in GR α . If no X-ray structure were available for GR α , then one could build a model for GR α using the available X-ray structures of PR and/or AR as templates. These theoretical models have some utility, but cannot be as accurate as a true X-ray structure, such as the X-ray structure disclosed here. Because of their limited accuracy, a

model for GR α will generally be less useful than an X-ray structure for the design of agonists, antagonists and modulators of GR α .

The solved GR α -ligand-co-activator crystal structure would provide structural details and insights necessary to design a modulator of GR α that maximizes preferred requirements for any modulator, i.e. potency and specificity. By exploiting the structural details obtained from a GR α -ligand-co-activator crystal structure, it would be possible to design a GR α modulator that, despite GR α 's similarity with other steroid receptors and nuclear receptors, exploits the unique structural features of the ligand binding domain of human GR α . A GR α modulator developed using structure-assisted design would take advantage of heretofore unknown GR α structural considerations and thus be more effective than a modulator developed using homology-based design. Potential or existent homology models cannot provide the necessary degree of specificity. A GR α modulator designed using the structural coordinates of a crystalline form of the ligand binding domain of GR α in complex with a ligand and a co-activator would also provide a starting point for the development of modulators of other nuclear receptors.

Although several journal articles have referred to GR mutants having "increased ligand efficacy" in cell-based assays, it has not been mentioned that such mutants could have improved solution properties so that they could provide a suitable reagent for purification, assay, and crystallization. See Garabedian & Yamamoto (1992) *Mol. Biol. Cell* 3: 1245-1257; Kralli, et al., (1995) *Proc. Natl. Acad. Sci.* 92: 4701-4705; Bohen (1995) *J. Biol. Chem.* 270: 29433-29438; Bohen (1998) *Mol. Cell. Biol.* 18: 3330-3339; Freeman et al., (2000) *Genes Dev.* 14: 422-434.

Indeed, it is well documented that GR associates with molecular chaperones (such as hsp90, hsc70, and p23). In the past, it has been considered that GR would either not be active or soluble if purified away from these binding partners. In fact, it has even been mentioned that GR must be in complex with hsp90 in order to adopt a high affinity steroid binding conformation. See Xu et al. (1998) *J. Biol. Chem.* 273: 13918-13924; Rajapandi et al. (2000) *J. Biol. Chem.* 275: 22597-22604.

Still other journal articles have reported *E.coli* expression of GST-GR, but also noted a failure to purify the purported polypeptide. See Ohara-Nemoto et al., (1990) *J. Steroid Biochem. Molec. Biol.* 37: 481-490; Caamano et al., (1994) *Annal. NY Acad. Sci.* 746: 68-77.

5 What is needed, therefore, is a purified, soluble GR α LBD polypeptide for use in structural studies, as well as methods for making the same. Such methods would also find application in the preparation of modified NRs in general.

What is also needed is a crystallized form of a GR α ligand binding domain, preferably in complex with a ligand and more preferably in complex with a ligand and a co-activator. Acquisition of crystals of the GR α ligand binding domain polypeptide permits the three-dimensional structure of a GR α ligand binding domain (LBD) polypeptide to be determined. Knowledge of the three dimensional structure can facilitate the design of modulators of GR-mediated activity. Such modulators can lead to therapeutic compounds to treat a wide range of conditions, including inflammation, tissue rejection, auto-immunity, malignancies such as leukemias and lymphomas, Cushing's syndrome, acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, polyarteritis nodosa, granulomatous polyarteritis, inhibition of myeloid cell lines, immune proliferation/apoptosis, HPA axis suppression and regulation, hypercortisolemia, modulation of the TH1/TH2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hyperglycemia, acute adrenal insufficiency, chronic primary adrenal insufficiency, secondary adrenal insufficiency, congenital adrenal hyperplasia, cerebral edema, thrombocytopenia, Little's syndrome, inflammatory bowel disease, systemic lupus erythematosus, polyarthritis nodosa, Wegener's granulomatosis, giant cell arteritis, rheumatoid arthritis, osteoarthritis, hay fever, allergic rhinitis, urticaria, angioneurotic edema, chronic obstructive pulmonary disease, asthma, tendonitis, bursitis, Crohn's disease, ulcerative colitis, autoimmune chronic active hepatitis, organ transplantation, hepatitis, cirrhosis, inflammatory scalp alopecia, panniculitis, psoriasis, discoid lupus erythematosus, inflamed cysts, atopic dermatitis, pyoderma gangrenosum, pemphigus vulgaris, bullous pemphigoid, systemic lupus erythematosus, dermatomyositis, herpes gestationis, eosinophilic fasciitis, relapsing polychondritis, inflammatory vasculitis, sarcoidosis, Sweet's disease, type 1 reactive leprosy, capillary hemangiomas,

contact dermatitis, atopic dermatitis, lichen planus, exfoliative dermatitis, erythema nodosum, acne, hirsutism, toxic epidermal necrolysis, erythema multiform, cutaneous T-cell lymphoma. Other applications of a GR modulator developed in accordance with the present invention can be employed to treat

5 Human Immunodeficiency Virus (HIV), cell apoptosis, and can be employed in treating cancerous conditions including, but not limited to, Kaposi's sarcoma, immune system activation and modulation, desensitization of inflammatory responses, IL-1 expression, natural killer cell development, lymphocytic leukemia, treatment of retinitis pigmentosa. Other applications for such a modulator

10 comprise modulating cognitive performance, memory and learning enhancement, depression, addiction, mood disorders, chronic fatigue syndrome, schizophrenia, stroke, sleep disorders, anxiety, immunostimulants, repressors, wound healing and a role as a tissue repair agent or in anti-retroviral therapy.

15 Summary of the Invention

A method of modifying a test NR polypeptide is disclosed. The method can comprise: providing a test NR polypeptide sequence having a characteristic that is targeted for modification; aligning the test NR polypeptide sequence with at least one reference NR polypeptide sequence for which an X-ray structure is

20 available, wherein the at least one reference NR polypeptide sequence has a characteristic that is desired for the test NR polypeptide; building a three-dimensional model for the test NR polypeptide using the three-dimensional coordinates of the X-ray structure(s) of the at least one reference polypeptide and its sequence alignment with the test NR polypeptide sequence; examining the

25 three-dimensional model of the test NR polypeptide for differences with the at least one reference polypeptide that are associated with the desired characteristic; and mutating at least one amino acid residue in the test NR polypeptide sequence located at a difference identified above to a residue associated with the desired characteristic, whereby the test NR polypeptide is modified.

30 A method of altering the solubility of a test NR polypeptide is also disclosed in accordance with the present invention. In a preferred embodiment, the method comprises: (a) providing a reference NR polypeptide sequence and a test NR polypeptide sequence; (b) comparing the reference NR polypeptide sequence and

the test NR polypeptide sequence to identify one or more residues in the test NR sequence that are more or less hydrophilic than a corresponding residue in the reference NR polypeptide sequence; and (c) mutating the residue in the test NR polypeptide sequence identified in step (b) to a residue having a different hydrophilicity, whereby the solubility of the test NR polypeptide is altered. Optionally, the reference NR polypeptide sequence is an AR or a PR sequence, and the test polypeptide sequence is a GR polypeptide sequence. Alternatively, the reference polypeptide sequence is a crystalline GR LBD. The comparing of step (b) is preferably by sequence alignment.

An isolated GR polypeptide comprising a mutation in a ligand binding domain, wherein the mutation alters the solubility of the ligand binding domain, is also disclosed. An isolated GR polypeptide, or functional portion thereof, having one or more mutations comprising a substitution of a hydrophobic amino acid residue by a hydrophilic amino acid residue in a ligand binding domain is also disclosed. Preferably, in each case, the mutation can be at a residue selected from the group consisting of V552, W557, F602, L636, Y648, W712, L741, L535, V538, C638, M691, V702, Y648, Y660, L685, M691, V702, W712, L733, Y764 and combinations thereof. More preferably, the mutation is selected from the group consisting of V552K, W557S, F602S, F602D, F602E, L636E, Y648Q, W712S, L741R, L535T, V538S, C638S, M691T, V702T, W712T and combinations thereof. Antibodies against such polypeptides are also disclosed, as are methods of detecting such polypeptides and methods of identifying substances that modulate the biological activity of such polypeptides.

An isolated nucleic acid molecule encoding a GR polypeptide comprising a mutation in a ligand binding domain, wherein the mutation alters the solubility of the ligand binding domain, or encoding a GR LBD polypeptide, or functional portion thereof, having one or more mutations comprising a substitution of a hydrophobic amino acid residue by a hydrophilic amino acid residue, is also disclosed. A chimeric gene, comprising the nucleic acid molecule operably linked to a heterologous promoter, a vector comprising the chimeric gene, and a host cell comprising the chimeric gene are also disclosed. Methods for detecting such a nucleic acid molecule are also disclosed.

A substantially pure GR α ligand binding domain polypeptide in crystalline form is disclosed. Preferably, the crystalline form has lattice constants of $a = b = 126.014 \text{ \AA}$, $c = 86.312 \text{ \AA}$, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 120^\circ$. Preferably, the crystalline form is a hexagonal crystalline form. More preferably, the crystalline form has a space group of P6₁. Even more preferably, the GR α ligand binding domain polypeptide has the F602S amino acid sequence shown in Example 2. Even more preferably, the GR α ligand binding domain has a crystalline structure further characterized by the coordinates corresponding to Table 4.

Preferably, the GR α ligand binding domain polypeptide is in complex with a ligand. Optionally, the crystalline form contains two GR α ligand binding domain polypeptides in the asymmetric unit. Preferably, the crystalline form is such that the three-dimensional structure of the crystallized GR α ligand binding domain polypeptide can be determined to a resolution of about 2.8 \AA or better. Even more preferably, the crystalline form contains one or more atoms having a molecular weight of 40 grams/mol or greater.

A method for determining the three-dimensional structure of a crystallized GR ligand binding domain polypeptide to a resolution of about 2.8 \AA or better, the method comprising: (a) crystallizing a GR ligand binding domain polypeptide; and (b) analyzing the GR ligand binding domain polypeptide to determine the three-dimensional structure of the crystallized GR ligand binding domain polypeptide, whereby the three-dimensional structure of a crystallized GR ligand binding domain polypeptide is determined to a resolution of about 2.8 \AA or better. Preferably, the analyzing is by X-ray diffraction. More preferably, the crystallization is accomplished by the hanging drop method, and wherein the GR α ligand binding domain is mixed with a reservoir.

A method of generating a crystallized GR ligand binding domain polypeptide, the method comprising: (a) incubating a solution comprising a GR ligand binding domain with a reservoir; and (b) crystallizing the GR ligand binding domain polypeptide using the hanging drop method, whereby a crystallized GR ligand binding domain polypeptide is generated.

A method of designing a modulator of a nuclear receptor, the method comprising: (a) designing a potential modulator of a nuclear receptor that will

make interactions with amino acids in the ligand binding site of the nuclear receptor based upon the atomic structure coordinates of a GR ligand binding domain polypeptide; (b) synthesizing the modulator; and (c) determining whether the potential modulator modulates the activity of the nuclear receptor, whereby a modulator of a nuclear receptor is designed.

A method of designing a modulator that selectively modulates the activity of a GR α polypeptide the method comprising: (a) obtaining a crystalline form of a GR α ligand binding domain polypeptide; (b) determining the three-dimensional structure of the crystalline form of the GR α ligand binding domain polypeptide; and (c) synthesizing a modulator based on the three-dimensional structure of the crystalline form of the GR α ligand binding domain polypeptide, whereby a modulator that selectively modulates the activity of a GR α polypeptide is designed. Preferably, the method further comprises contacting a GR α ligand binding domain polypeptide with the potential modulator; and assaying the GR α ligand binding domain polypeptide for binding of the potential modulator, for a change in activity of the GR α ligand binding domain polypeptide, or both. More preferably, the crystalline form is in orthorhombic form. Even more preferably, the crystals are such that the three-dimensional structure of the crystallized GR α ligand binding domain polypeptide can be determined to a resolution of about 2.8 Å or better.

A method of screening a plurality of compounds for a modulator of a GR ligand binding domain polypeptide, the method comprising: (a) providing a library of test samples; (b) contacting a GR ligand binding domain polypeptide with each test sample; (c) detecting an interaction between a test sample and the GR ligand binding domain polypeptide; (d) identifying a test sample that interacts with the GR ligand binding domain polypeptide; and (e) isolating a test sample that interacts with the GR ligand binding domain polypeptide, whereby a plurality of compounds is screened for a modulator of a GR ligand binding domain polypeptide. Preferably, the test samples are bound to a substrate, and more preferably, the test samples are synthesized directly on a substrate. The GR ligand binding domain polypeptide can be in soluble or crystalline form.

A method for identifying a GR modulator is also disclosed. In a preferred

embodiment, the method comprises: (a) providing atomic coordinates of a GR ligand binding domain to a computerized modeling system; and (b) modeling ligands that fit spatially into the binding pocket of the GR ligand binding domain to thereby identify a GR modulator, whereby a GR modulator is identified.

- 5 Preferably, the method further comprises identifying in an assay for GR-mediated activity a modeled ligand that increases or decreases the activity of the GR.

A method of identifying modulator that selectively modulates the activity of a GR α polypeptide compared to other GR polypeptides, the method comprising: (a) providing atomic coordinates of a GR α ligand binding domain to a
10 computerized modeling system; and (b) modeling a ligand that fits into the binding pocket of a GR α ligand binding domain and that interacts with conformationally constrained residues of a GR α conserved among GR subtypes, whereby a modulator that selectively modulates the activity of a GR α polypeptide compared to other polypeptides is identified. Preferably, the method further comprises
15 identifying in a biological assay for GR α activity a modeled ligand that selectively binds to GR α and increases or decreases the activity of said GR α .

A method of designing a modulator of a GR polypeptide, the method comprising: (a) selecting a candidate GR ligand; (b) determining which amino acid or amino acids of a GR polypeptide interact with the ligand using a three-
20 dimensional model of a crystallized protein comprising a GR α LBD; (c) identifying in a biological assay for GR activity a degree to which the ligand modulates the activity of the GR polypeptide; (d) selecting a chemical modification of the ligand wherein the interaction between the amino acids of the GR polypeptide and the ligand is predicted to be modulated by the chemical modification; (e) synthesizing
25 a chemical compound with the selected chemical modification to form a modified ligand; (f) contacting the modified ligand with the GR polypeptide; (g) identifying in a biological assay for GR activity a degree to which the modified ligand modulates the biological activity of the GR polypeptide; and (h) comparing the biological activity of the GR polypeptide in the presence of modified ligand with the biological
30 activity of the GR polypeptide in the presence of the unmodified ligand, whereby a modulator of a GR polypeptide is designed. Preferably, the GR polypeptide is a GR α polypeptide. More preferably, the three-dimensional model of a crystallized

protein is a GR α LBD polypeptide with a bound ligand. Optionally, the method further comprises repeating steps (a) through (f), if the biological activity of the GR polypeptide in the presence of the modified ligand varies from the biological activity of the GR polypeptide in the presence of the unmodified ligand.

5 An assay method for identifying a compound that inhibits binding of a ligand to a GR polypeptide, the assay method comprising: (a) designing a test inhibitor compound based on the three dimensional atomic coordinates of GR; (b) incubating a GR polypeptide with a ligand in the presence of a test inhibitor compound; (c) determining an amount of ligand that is bound to the GR
10 polypeptide, wherein decreased binding of ligand to the GR protein in the presence of the test inhibitor compound relative to binding of ligand in the absence of the test inhibitor compound is indicative of inhibition; and (d) identifying the test compound as an inhibitor of ligand binding if decreased ligand binding is observed, whereby a compound that inhibits binding of a ligand to a GR
15 polypeptide is identified.

A method of identifying a NR modulator that selectively modulates the biological activity of one NR compared to GR α is also disclosed. The method comprises: (a) providing an atomic structure coordinate set describing a GR α ligand binding domain structure and at least one other atomic structure coordinate
20 set describing a NR ligand binding domain, each ligand binding domain comprising a ligand binding site; (b) comparing the atomic structure coordinate sets to identify at least one difference between the sets; (c) designing a candidate ligand predicted to interact with the difference of step (b); (d) synthesizing the candidate ligand; and (e) testing the synthesized candidate ligand for an ability to
25 selectively modulate a NR as compared to GR α , whereby a NR modulator that selectively modulates the biological activity NR compared to GR α is identified.

Accordingly, it is an object of the present invention to provide a three dimensional structure of the ligand binding domain of a GR. The object is achieved in whole or in part by the present invention.

30 An object of the invention having been stated hereinabove, other objects will be evident as the description proceeds, when taken in connection with the accompanying Drawings and Laboratory Examples as best described hereinbelow.

Brief Description of the Drawings

Figure 1A depicts *E. coli* expression of mutant 6xHisGST-GR(521-777) F602S (SEQ ID NO:12) via SDS-PAGE. Staining was accomplished using the commercially available PROBLUE product.

5 Figure 1B depicts *E. coli* expression of mutant 6xHisGST-GR(521-777) F602D (SEQ ID NO:14) via SDS-PAGE. Staining was accomplished using the commercially available PROBLUE product.

10 Figure 1C depicts purification of *E. coli* expressed GR(521-777)F602S (SEQ ID NO:12) via SDS-PAGE. Staining was accomplished using the commercially available PROBLUE product.

Figure 1D shows the partial purification of *E. Coli* expressed GR (521-777) for several mutants isolated by the LacI Fusion system.

Figures 2A-2C depict characterization of GR binding to dexamethasone and the TIF2 LXXLL (SEQ ID NO:18) motif.

15 Figure 2A is a graph depicting the binding of 10 nM fluorescein dexamethasone to varied concentrations of GST-GR LBD (F602S) 521-777 (circles), GR LBD (F602S) 521-777 (triangles) and GR LBD (F602S) 521-777 in the presence of 100 uM unlabeled dexamethasone (squares) as measured by fluorescence polarization.

20 Figure 2B is a graph depicting ligand-dependent binding of TIF2 LXXLL(SEQ ID NO:18) motif to GR LBD. The binding of varied concentrations of GST-GR LBD (F602S) 521-777 to immobilized TIF2 732-756 peptide (SEQ ID NO:17) in the presence of a five-fold excess of dexamethasone (triangles), RU486 (squares) and no compound (circles) was measured by surface plasmon resonance. Each point is the average of two determinations.

25 Figure 2C is a graph depicting that TIF2 coactivator peptide enhances stability of GR dexamethasone binding activity. The effect of 25 uM coactivator peptide TIF2 732-756 (diamonds) or no peptide (squares) on the binding of GST-GR LBD (F602S) 521-777 to 10 nM fluorescein dexamethasone with time is determined by fluorescence polarization.

30 Figure 3A is a worm/ribbon diagram depicting the overall arrangement of the GR LBD dimers. Two GR LBDs are shown in white and gray worm

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representation. TIF2 peptides are shown in gray ribbon and the two dexamethasone ligands are shown in space filling.

Figure 3B is a worm/ribbon diagram depicting one orientation of the GR/TIF2/Dex complex. TIF peptide is shown in ribbon and GR is shown in worm.

5 The AF2 helix of the GR is shown in gray worm. The key structural elements are marked and are described herein below.

Figure 3C is a worm/ribbon diagram depicting a second orientation of the GR/TIF2/DEX complex. TIF2 peptide is shown in ribbon and GR is shown in worm. The AF2 helix of GR is shown in gray worm. The key structural elements
10 are marked and are described herein below.

Figures 4A and 4B depict the overlap of the GR LBD with the AR LBD (Figure 4A) and the PR LBD (Figure 4B). The GR is in thick line. AR and PR are in the thin line. Only the backbone C alpha atoms are shown.

Figure 5 is a sequence alignment of steroid receptors, particularly an
15 alignment of the F602S GR α sequence (SEQ ID NO:31) with MR(SEQ ID NO:26), PR(SEQ ID NO:27), AR(SEQ ID NO:28), ER α (SEQ ID NO:29), and ER β (SEQ ID NO:30). Residues that lie within 5.0 angstroms of the ligand are identified with small square boxes around the one-letter amino acid code. The ligands used for this calculation are dexamethasone (for GR), progesterone (for PR),
20 dihydrotestosterone (for AR), estradiol (for ER α) and genistein (for ER β). The alpha-helices and beta-strands observed in the X-ray structures are identified by the larger boxes and captions. Note that the secondary structure of MR is not publicly known at this time, and thus is not annotated in the Figure. More than one structure is available for PR, AR, ER α and ER β , and, in some cases, the
25 alpha-helices have different endpoints in these different X-ray structures. The variation in the alpha-helices is indicated here by using boxes with thicker and thinner linewidths, where the thicker linewidth box encompasses residues that adopt the same secondary structure in all available X-ray structures, and thinner linewidth boxes encompass residues that adopt an alpha-helical structure in some
30 but not all X-ray structures. The secondary structures were determined by graphical examination of the X-ray structures.

Figure 6A depicts the GR ligand binding pocket. The GR LBD is shown in a worm representation and the pocket is shown with a white surface.

Figure 6B is a diagram that depicts surfaces at the GR-dexamethasone interface. The electron density is calculated with Fo coefficient and shown at a one sigma cutoff. Key residues surrounding the ligand are also labeled, as described herein below.

5 Figure 7 is a diagram of molecular interactions between GR and dexamethasone. Both Van der Waals contacts and hydrogen bonds are indicated with dotted lines.

10 Figure 8 is a wire frame diagram showing the structure around the F602 mutation in the GR α LBD polypeptide. The lipophilic F602 side-chain of the wild-type GR α protein would be located in a hydrophilic environment and could destabilize the protein. Changing the phenylalanine (F) to a serine (S) allows the S602 side-chain and NH group to make direct hydrogen bonds with two water molecules (1H₂O and 2H₂O). Other residues involved with the two water molecules are also shown and are described herein below.

15

Brief Description of Sequences in the Sequence Listing

SEQ ID NOs:1 and 2 are, respectively, a DNA sequence encoding a wild type full-length human glucocorticoid receptor (GenBank Accession No. 31679) and the amino acid sequence (GenBank Accession No. 121069) of a human glucocorticoid receptor encoded by the DNA sequence.

20 SEQ ID NOs:3 and 4 are, respectively, a DNA sequence encoding a F602S full-length human glucocorticoid receptor and the amino acid sequence of a human glucocorticoid receptor encoded by the DNA sequence.

25 SEQ ID NOs:5 and 6 are, respectively, a DNA sequence encoding a F602D full-length human glucocorticoid receptor and the amino acid sequence of a human glucocorticoid receptor encoded by the DNA sequence.

30 SEQ ID NOs:7 and 8 are, respectively, a DNA sequence encoding a preferred embodiment of a full-length human glucocorticoid receptor of the present invention and the amino acid sequence of a human glucocorticoid receptor encoded by the DNA sequence. These sequences thus include variable amino acids at the following locations: V552, W557, F602, L636, Y648, W712, L741, L535, V538, C638, M691, V702, Y648, Y660, L685, M691, V702, W712, L733, and Y764, thus reflecting the mutagenesis approach of the present

invention disclosed herein below. Thus, a full length human glucocorticoid receptor of the present invention can include a mutation at any one of these residues, and/or at any combination of these residues.

5 SEQ ID NOs:9 and 10 are, respectively, a DNA sequence encoding a wild type ligand binding domain of a human glucocorticoid receptor and the amino acid sequence of a human glucocorticoid receptor encoded by the DNA sequence.

10 SEQ ID NOs:11 and 12 are, respectively, a DNA sequence encoding a ligand binding domain (residues 521-777) of a human glucocorticoid receptor containing a phenylalanine to serine mutation at residue 602 and the amino acid sequence of a human glucocorticoid receptor encoded by the DNA sequence.

15 SEQ ID NOs:13 and 14 are, respectively, a DNA sequence encoding a ligand binding domain (residues 521-777) of a human glucocorticoid receptor containing a phenylalanine to aspartic acid mutation at residue 602 and the amino acid sequence of a human glucocorticoid receptor encoded by the DNA sequence.

20 SEQ ID NOs:15 and 16 are, respectively, a DNA sequence encoding a preferred embodiment of a ligand binding domain of a human glucocorticoid receptor of the present invention and the amino acid sequence of a human glucocorticoid receptor encoded by the DNA sequence. These sequences thus include variable amino acids at the following locations: V552, W557, F602, L636, Y648, W712, L741, L535, V538, C638, M691, V702, Y648, Y660, L685, M691, V702, W712, L733, and Y764, thus reflecting the mutagenesis approach of the present invention disclosed herein below. Thus, a ligand binding domain of a human glucocorticoid receptor of the present invention can include a mutation at
25 any one of these residues, and/or at any combination of these residues.

SEQ ID NO:17 is an amino acid sequence of amino acid residues 732-756 of the human TIF2 protein.

SEQ ID NO:18 is an LXXLL motif of the human TIF2 protein.

30 SEQ ID NOs:19-20 are oligonucleotide primers used to engineer a polyhistidine tag in frame to the sequence encoding glutathione S-transferase (GST).

SEQ ID NO:21 is the resulting amino acid sequence of the modified GST.

SEQ ID NOs:22-25 are oligonucleotide primers used in the mutagenesis approach of the present invention.

5 SEQ ID NOs:26-31 are the ligand binding domain polypeptides of MR(SEQ ID NO:26), PR(SEQ ID NO:27), AR(SEQ ID NO:28), ER α (SEQ ID NO:29), ER β (SEQ ID NO:30), and F602S GR α (SEQ ID NO:31) respectively. All of these sequences are also shown in Figure 5. Note that the GR α sequence shown of SEQ ID NO:31 starts at residue 527, whereas the F602S sequence of SEQ ID NO:12 starts at residue 521.

10 SEQ ID NO:32 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor containing a phenylalanine to serine mutation at residue 602, wherein the first two residues comprise a thrombin cleavage site encoded by vector.

15 SEQ ID NO: 33 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor comprising a W557R mutation.

SEQ ID NO: 34 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor comprising a Q615L mutation.

20 SEQ ID NO: 35 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor comprising a Q615H mutation.

SEQ ID NO: 36 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor comprising a A574T mutation.

25 SEQ ID NO: 37 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor comprising a L620M mutation.

30 SEQ ID NO: 38 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor comprising the double mutation F602L/A580T.

SEQ ID NO: 39 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor comprising the double mutation L563F/G583C.

SEQ ID NO: 40 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor comprising the double mutation L664H/M752T.

5 SEQ ID NO: 41 is an amino acid sequence of a ligand binding domain (residues 521-777) of a human glucocorticoid receptor comprising the double mutation L563F/T744N.

Detailed Description of the Invention

10 The present invention provides for the generation of NR, SR and GR polypeptides and NR, SR or GR mutants (preferably GR α and GR α LBD mutants), and the ability to solve the crystal structures of those that crystallize. Indeed, a GR α LBD having a point mutation was crystallized and solved in one aspect of the present invention. Thus, an aspect of the present invention involves the use of both targeted and random mutagenesis of the GR gene for the
15 production of a recombinant protein with improved solution characteristics for the purpose of crystallization, characterization of biologically relevant protein-protein interactions, and compound screening assays. The present invention, relating to GR LBD F602S and other LBD mutations, shows that GR can be overexpressed using an *E.coli* expression system and that active GR protein can be purified,
20 assayed, and crystallized.

Until disclosure of the present invention presented herein, the ability to obtain crystalline forms of the ligand binding domain of GR α has not been realized. And until disclosure of the present invention presented herein, a detailed three-dimensional crystal structure of a GR α LBD polypeptide has not been
25 solved.

In addition to providing structural information, crystalline polypeptides provide other advantages. For example, the crystallization process itself further purifies the polypeptide, and satisfies one of the classical criteria for homogeneity. In fact, crystallization frequently provides unparalleled purification quality, removing impurities that are not removed by other purification methods such as
30 HPLC, dialysis, conventional column chromatography, and other methods. Moreover, crystalline polypeptides are sometimes stable at ambient temperatures and free of protease contamination and other degradation associated with solution

storage. Crystalline polypeptides can also be useful as pharmaceutical preparations. Finally, crystallization techniques in general are largely free of problems such as denaturation associated with other stabilization methods (e.g., lyophilization). Once crystallization has been accomplished, crystallographic data provides useful structural information that can assist the design of compounds that can serve as modulators (e.g. agonists or antagonists), as described herein below. In addition, the crystal structure provides information useful to map a receptor binding domain, which can then be mimicked by a chemical entity that can serve as an antagonist or agonist.

I. Definitions

Following long-standing patent law convention, the terms "a" and "an" mean "one or more" when used in this application, including the claims.

As used herein, the term "agonist" means an agent that supplements or potentiates the bioactivity of a functional GR gene or protein or of a polypeptide encoded by a gene that is up- or down-regulated by a GR polypeptide and/or a polypeptide encoded by a gene that contains a GR binding site or response element in its promoter region. By way of specific example, an "agonist" is a compound that interacts with the steroid hormone receptor to promote a transcriptional response. An agonist can induce changes in a receptor that places the receptor in an active conformation that allows them to influence transcription, either positively or negatively. There can be several different ligand-induced changes in the receptor's conformation. The term "agonist" specifically encompasses partial agonists.

As used herein, the terms " α -helix", "alpha-helix" and "alpha helix" are used interchangeably and mean the conformation of a polypeptide chain wherein the polypeptide backbone is wound around the long axis of the molecule in a left-handed or right-handed direction, and the R groups of the amino acids protrude outward from the helical backbone, wherein the repeating unit of the structure is a single turnoff the helix, which extends about 0.56 nm along the long axis.

As used herein, the term "antagonist" means an agent that decreases or inhibits the bioactivity of a functional GR gene or protein, or that supplements or potentiates the bioactivity of a naturally occurring or engineered non-functional GR

gene or protein. Alternatively, an antagonist can decrease or inhibit the bioactivity of a functional gene or polypeptide encoded by a gene that is up- or down-regulated by a GR polypeptide and/or contains a GR binding site or response element in its promoter region. An antagonist can also supplement or potentiate

5 the bioactivity of a naturally occurring or engineered non-functional gene or polypeptide encoded by a gene that is up- or down-regulated by a GR polypeptide, and/or contains a GR binding site or response element in its promoter region. By way of specific example, an "antagonist" is a compound that interacts with the steroid hormone receptor to inhibit a transcriptional response.

10 An antagonist can bind to a receptor but fail to induce conformational changes that alter the receptor's transcriptional regulatory properties or physiologically relevant conformations. Binding of an antagonist can also block the binding and therefore the actions of an agonist. The term "antagonist" specifically encompasses partial antagonists.

15 As used herein, the terms " β -sheet", "beta-sheet" and "beta sheet" are used interchangeably and mean the conformation of a polypeptide chain stretched into an extended zig-zig conformation. Portions of polypeptide chains that run "parallel" all run in the same direction. Polypeptide chains that are "antiparallel" run in the opposite direction from the parallel chains.

20 As used herein, the terms "binding pocket of the GR ligand binding domain", "GR ligand binding pocket" and "GR binding pocket" are used interchangeably, and refer to the large cavity within the GR ligand binding domain where a ligand can bind. This cavity can be empty, or can contain water molecules or other molecules from the solvent, or can contain ligand atoms. The

25 main binding pocket is the region of space encompassed the residues depicted Figure 7. The binding pocket also includes regions of space near the "main" binding pocket that not occupied by atoms of GR but that are near the "main" binding pocket, and that are contiguous with the "main" binding pocket.

As used herein, the term "biological activity" means any observable effect

30 flowing from interaction between a GR polypeptide and a ligand. Representative, but non-limiting, examples of biological activity in the context of the present invention include transcription regulation, ligand binding and peptide binding.

As used herein, the terms "candidate substance" and "candidate compound" are used interchangeably and refer to a substance that is believed to interact with another moiety, for example a given ligand that is believed to interact with a complete, or a fragment of, a GR polypeptide, and which can be subsequently evaluated for such an interaction. Representative candidate substances or compounds include xenobiotics such as drugs and other therapeutic agents, carcinogens and environmental pollutants, natural products and extracts, as well as endobiotics such as glucocorticosteroids, steroids, fatty acids and prostaglandins. Other examples of candidate compounds that can be investigated using the methods of the present invention include, but are not restricted to, agonists and antagonists of a GR polypeptide, toxins and venoms, viral epitopes, hormones (e.g., glucocorticosteroids, opioid peptides, steroids, etc.), hormone receptors, peptides, enzymes, enzyme substrates, co-factors, lectins, sugars, oligonucleotides or nucleic acids, oligosaccharides, proteins, small molecules and monoclonal antibodies.

As used herein, the terms "cells," "host cells" or "recombinant host cells" are used interchangeably and mean not only to the particular subject cell, but also to the progeny or potential progeny of such a cell. Because certain modifications can occur in succeeding generations due to either mutation or environmental influences, such progeny might not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

As used herein, the terms "chimeric protein" or "fusion protein" are used interchangeably and mean a fusion of a first amino acid sequence encoding a GR polypeptide with a second amino acid sequence defining a polypeptide domain foreign to, and not homologous with, any domain of a GR polypeptide. A chimeric protein can include a foreign domain that is found in an organism that also expresses the first protein, or it can be an "interspecies" or "intergenic" fusion of protein structures expressed by different kinds of organisms. In general, a fusion protein can be represented by the general formula X—GR—Y, wherein GR represents a portion of the protein which is derived from a GR polypeptide, and X and Y are independently absent or represent amino acid sequences which are not related to a GR sequence in an organism, which includes naturally occurring mutants.

As used herein, the term "co-activator" means an entity that has the ability to enhance transcription when it is bound to at least one other entity. The association of a co-activator with an entity has the ultimate effect of enhancing the transcription of one or more sequences of DNA. In the context of the present invention, transcription is preferably nuclear receptor-mediated. By way of specific example, in the present invention TIF2 (the human analog of mouse glucocorticoid receptor interaction protein 1 (GRIP1)) can bind to a site on the glucocorticoid receptor, an event that can enhance transcription. TIF2 is therefore a co-activator of the glucocorticoid receptor. Other GR co-activators can include SRC1.

As used herein, the term "co-repressor" means an entity that has the ability to repress transcription when it is bound to at least one other entity. In the context of the present invention, transcription is preferably nuclear receptor-mediated. The association of a co-repressor with an entity has the ultimate effect of repressing the transcription of one or more sequences of DNA.

As used herein, the term "crystal lattice" means the array of points defined by the vertices of packed unit cells.

As used herein, the term "detecting" means confirming the presence of a target entity by observing the occurrence of a detectable signal, such as a radiologic or spectroscopic signal that will appear exclusively in the presence of the target entity.

As used herein, the term "DNA segment" means a DNA molecule that has been isolated free of total genomic DNA of a particular species. In a preferred embodiment, a DNA segment encoding a GR polypeptide refers to a DNA segment that comprises any of the odd numbered SEQ ID NOs:1-16, but can optionally comprise fewer or additional nucleic acids, yet is isolated away from, or purified free from, total genomic DNA of a source species, such as *Homo sapiens*. Included within the term "DNA segment" are DNA segments and smaller fragments of such segments, and also recombinant vectors, including, for example, plasmids, cosmids, phages, viruses, and the like.

As used herein, the term "DNA sequence encoding a GR polypeptide" can refer to one or more coding sequences within a particular individual. Moreover, certain differences in nucleotide sequences can exist between individual

organisms, which are called alleles. It is possible that such allelic differences might or might not result in differences in amino acid sequence of the encoded polypeptide yet still encode a protein with the same biological activity. As is well known, genes for a particular polypeptide can exist in single or multiple copies within the genome of an individual. Such duplicate genes can be identical or can have certain modifications, including nucleotide substitutions, additions or deletions, all of which still code for polypeptides having substantially the same activity.

As used herein, the phrase "enhancer-promoter" means a composite unit that contains both enhancer and promoter elements. An enhancer-promoter is operatively linked to a coding sequence that encodes at least one gene product.

As used herein, the term "expression" generally refers to the cellular processes by which a biologically active polypeptide is produced.

As used herein, the term "gene" is used for simplicity to refer to a functional protein, polypeptide or peptide encoding unit. As will be understood by those in the art, this functional term includes both genomic sequences and cDNA sequences. Preferred embodiments of genomic and cDNA sequences are disclosed herein.

As used herein, the term "glucocorticoid" means a steroid hormone glucocorticoid. "Glucocorticoids" are agonists for the glucocorticoid receptor. Compounds which mimic glucocorticoids are also be defined as glucocorticoid receptor agonists. A preferred glucocorticoid receptor agonist is dexamethasone. Other common glucocorticoid receptor agonists include cortisol, cortisone, prednisolone, prednisone, methylprednisolone, trimcinolone, hydrocortisone, and corticosterone. As used herein, glucocorticoid is intended to include, for example, the following generic and brand name corticosteroids: cortisone (CORTONE ACETATE, ADRESON, ALTESONA, CORTELAN, CORTISTAB, CORTISYL, CORTOGEN, CORTONE, SCHEROSON); dexamethasone—oral (DECADRON-ORAL, DEXAMETH, DEXONE, HEXADROL-ORAL, DEXAMETHASONE INTENSOL, DEXONE 0.5, DEXONE 0.75, DEXONE 1.5, DEXONE 4); hydrocortisone—oral (CORTEF, HYDROCORTONE); hydrocortisone cypionate (CORTEF ORAL SUSPENSION); methylprednisolone—oral (MEDROL-ORAL); prednisolone—oral (PRELONE, DELTA-CORTEF, PEDIAPRED, ADNISOLONE,

CORTALONE, DELTACORTIL, DELTASOLONE, DELTASTAB, DI-ADRESON
F, ENCORTOLONE, HYDROCORTANCYL, MEDISOLONE, METICORTELONE,
OPREDSONE, PANAAFCORTELONE, PRECORTISYL, PRENISOLONA,
SCHERISOLONA, SCHERISOLONE); prednisone (DELTASONE, LIQUID PRED,
5 METICORTEN, ORASONE 1, ORASONE 5, ORASONE 10, ORASONE 20,
ORASONE 50, PREDNICEN-M, PREDNISON INTENSOL, STERAPRED,
STERAPRED DS, ADASONE, CARTANCYL, COLISONE, CORDROL, CORTAN,
DACORTIN, DECORTIN, DECORTISYL, DELCORTIN, DELLACORT, DELTA-
DOME, DELTACORTENE, DELTISONA, DIADRESON, ECONOSONE,
10 ENCORTON, FERNISONE, NISONA, NOVOPREDNISON, PANAFECORT,
PANASOL, PARACORT, PARMENISON, PEHACORT, PREDELIN,
PREDNICORT, PREDNICOT, PREDNIDIB, PREDNIMENT, RECTODELT,
ULTRACORTEN, WINPRED); triamcinolone--oral (KENACORT, ARISTOCORT,
ATOLONE, SHOLOG A, TRAMACORT-D, TRI-MED, TRIAMCOT, TRISTO-PLEX,
15 TRYLONE D, U-TRI-LONE).

As used herein, the term "glucocorticoid receptor," abbreviated herein as
"GR," means the receptor for a steroid hormone glucocorticoid. A glucocorticoid
receptor is a steroid receptor and, consequently, a nuclear receptor, since steroid
receptors are a subfamily of the superfamily of nuclear receptors. The term "GR"
20 means any polypeptide sequence that can be aligned with human GR such that at
least 70%, preferably at least 75%, of the amino acids are identical to the
corresponding amino acid in the human GR. The term "GR" also encompasses
nucleic acid sequences where the corresponding translated protein sequence can
be considered to be a GR. The term "GR" includes invertebrate homologs,
25 whether now known or hereafter identified; preferably, GR nucleic acids and
polypeptides are isolated from eukaryotic sources. "GR" further includes
vertebrate homologs of GR family members, including, but not limited to,
mammalian and avian homologs. Representative mammalian homologs of GR
family members include, but are not limited to, murine and human homologs.
30 "GR" specifically encompasses all GR isoforms, including GR α and GR β . GR β is
a splicing variant with 100% identity to GR α , except at the C-terminus, where 50
residues in GR α have been replaced with 15 residues in GR β .

As used herein, the terms "GR gene product", "GR protein", "GR polypeptide", and "GR peptide" are used interchangeably and mean peptides having amino acid sequences which are substantially identical to native amino acid sequences from the organism of interest and which are biologically active in that they comprise all or a part of the amino acid sequence of a GR polypeptide, or cross-react with antibodies raised against a GR polypeptide, or retain all or some of the biological activity (e.g., DNA or ligand binding ability and/or transcriptional regulation) of the native amino acid sequence or protein. Such biological activity can include immunogenicity. Representative embodiments are set forth in any even numbered SEQ ID NOs:2-16. The terms "GR gene product", "GR protein", "GR polypeptide", and "GR peptide" also include analogs of a GR polypeptide. By "analog" is intended that a DNA or peptide sequence can contain alterations relative to the sequences disclosed herein, yet retain all or some of the biological activity of those sequences. Analogs can be derived from genomic nucleotide sequences as are disclosed herein or from other organisms, or can be created synthetically. Those skilled in the art will appreciate that other analogs, as yet undisclosed or undiscovered, can be used to design and/or construct GR analogs. There is no need for a "GR gene product", "GR protein", "GR polypeptide", or "GR peptide" to comprise all or substantially all of the amino acid sequence of a GR polypeptide gene product. Shorter or longer sequences are anticipated to be of use in the invention; shorter sequences are herein referred to as "segments". Thus, the terms "GR gene product", "GR protein", "GR polypeptide", and "GR peptide" also include fusion or recombinant GR polypeptides and proteins comprising sequences of the present invention. Methods of preparing such proteins are disclosed herein and are known in the art.

As used herein, the terms "GR gene" and "recombinant GR gene" mean a nucleic acid molecule comprising an open reading frame encoding a GR polypeptide of the present invention, including both exon and (optionally) intron sequences.

As used herein, "hexagonal unit cell" means a unit cell wherein $a = b \neq c$; and $\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$. The vectors a , b and c describe the unit cell edges and the angles α , β , and γ describe the unit cell angles. In a preferred embodiment of the present invention, the unit cell has lattice constants of $a = b = 126.014 \text{ \AA}$, $c =$

86.312 Å, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 120^\circ$. While preferred lattice constants are provided, a crystalline polypeptide of the present invention also comprises variations from the preferred lattice constants, wherein the variations range from about one to about two percent. Thus, for example, a crystalline polypeptide of
5 the present invention can also comprise lattice constants of about 125 or about 127.

As used herein, the term "hybridization" means the binding of a probe molecule, a molecule to which a detectable moiety has been bound, to a target sample.

10 As used herein, the term "interact" means detectable interactions between molecules, such as can be detected using, for example, a yeast two hybrid assay. The term "interact" is also meant to include "binding" interactions between molecules. Interactions can, for example, be protein-protein or protein-nucleic acid in nature.

15 As used herein, the term "intron" means a DNA sequence present in a given gene that is not translated into protein.

As used herein, the term "isolated" means oligonucleotides substantially free of other nucleic acids, proteins, lipids, carbohydrates or other materials with which they can be associated, such association being either in cellular material or
20 in a synthesis medium. The term can also be applied to polypeptides, in which case the polypeptide will be substantially free of nucleic acids, carbohydrates, lipids and other undesired polypeptides.

As used herein, the term "labeled" means the attachment of a moiety, capable of detection by spectroscopic, radiologic or other methods, to a probe
25 molecule.

As used herein, the term "modified" means an alteration from an entity's normally occurring state. An entity can be modified by removing discrete chemical units or by adding discrete chemical units. The term "modified" encompasses detectable labels as well as those entities added as aids in purification.

30 As used herein, the term "modulate" means an increase, decrease, or other alteration of any or all chemical and biological activities or properties of a wild-type or mutant GR polypeptide, preferably a wild-type or mutant GR polypeptide. The term "modulation" as used herein refers to both upregulation (i.e., activation or

stimulation) and downregulation (i.e. inhibition or suppression) of a response, and includes responses that are upregulated in one cell type or tissue, and down-regulated in another cell type or tissue.

As used herein, the term "molecular replacement" means a method that
5 involves generating a preliminary model of the wild-type GR ligand binding domain, or a GR mutant crystal whose structure coordinates are unknown, by orienting and positioning a molecule or model whose structure coordinates are known (e.g., a nuclear receptor) within the unit cell of the unknown crystal so as best to account for the observed diffraction pattern of the unknown crystal.
10 Phases can then be calculated from this model and combined with the observed amplitudes to give an approximate Fourier synthesis of the structure whose coordinates are unknown. This, in turn, can be subject to any of the several forms of refinement to provide a final, accurate structure of the unknown crystal. See, e.g., Lattman, (1985) *Method Enzymol.*, 115: 55-77; Rossmann, ed, (1972) The Molecular Replacement Method, Gordon & Breach, New York. Using the structure
15 coordinates of the ligand binding domain of GR provided by this invention, molecular replacement can be used to determine the structure coordinates of a crystalline mutant or homologue of the GR ligand binding domain, or of a different crystal form of the GR ligand binding domain.

20 As used herein, the term "mutation" carries its traditional connotation and means a change, inherited, naturally occurring or introduced, in a nucleic acid or polypeptide sequence, and is used in its sense as generally known to those of skill in the art.

As used herein, the term "nuclear receptor", occasionally abbreviated
25 herein as "NR", means a member of the superfamily of receptors that comprises at least the subfamilies of steroid receptors, thyroid hormone receptors, retinoic acid receptors and vitamin D receptors. Thus, a given nuclear receptor can be further classified as a member of a subfamily while retaining its status as a nuclear receptor.

30 As used herein, the phrase "operatively linked" means that an enhancer-promoter is connected to a coding sequence in such a way that the transcription of that coding sequence is controlled and regulated by that enhancer-promoter. Techniques for operatively linking an enhancer-promoter to a coding sequence

are well known in the art; the precise orientation and location relative to a coding sequence of interest is dependent, *inter alia*, upon the specific nature of the enhancer-promoter.

As used herein, the term "partial agonist" means an entity that can bind to a
5 receptor and induce only part of the changes in the receptors that are induced by agonists. The differences can be qualitative or quantitative. Thus, a partial agonist can induce some of the conformation changes induced by agonists, but not others, or it can only induce certain changes to a limited extent.

As used herein, the term "partial antagonist" means an entity that can bind
10 to a receptor and inhibit only part of the changes in the receptors that are induced by antagonists. The differences can be qualitative or quantitative. Thus, a partial antagonist can inhibit some of the conformation changes induced by an antagonist, but not others, or it can inhibit certain changes to a limited extent.

As used herein, the term "polypeptide" means any polymer comprising any
15 of the 20 protein amino acids, regardless of its size. Although "protein" is often used in reference to relatively large polypeptides, and "peptide" is often used in reference to small polypeptides, usage of these terms in the art overlaps and varies. The term "polypeptide" as used herein refers to peptides, polypeptides and proteins, unless otherwise noted. As used herein, the terms "protein",
20 "polypeptide" and "peptide" are used interchangeably herein when referring to a gene product.

As used herein, the term "primer" means a sequence comprising two or more deoxyribonucleotides or ribonucleotides, preferably more than three, and more preferably more than eight and most preferably at least about 20 nucleotides
25 of an exonic or intronic region. Such oligonucleotides are preferably between ten and thirty bases in length.

As used herein, the term "sequencing" means the determining the ordered linear sequence of nucleic acids or amino acids of a DNA or protein target sample, using conventional manual or automated laboratory techniques.

As used herein, the term "space group" means the arrangement of
30 symmetry elements of a crystal.

As used herein, the term "steroid receptor" means a nuclear receptor that can bind or associate with a steroid compound. Steroid receptors are a subfamily

of the superfamily of nuclear receptors. The subfamily of steroid receptors comprises glucocorticoid receptors and, therefore, a glucocorticoid receptor is a member of the subfamily of steroid receptors and the superfamily of nuclear receptors.

5 As used herein, the terms "structure coordinates" and "structural coordinates" mean mathematical coordinates derived from mathematical equations related to the patterns obtained on diffraction of a monochromatic beam of X-rays by the atoms (scattering centers) of a molecule in crystal form. The diffraction data are used to calculate an electron density map of the repeating unit
10 of the crystal. The electron density maps are used to establish the positions of the individual atoms within the unit cell of the crystal.

Those of skill in the art understand that a set of coordinates determined by X-ray crystallography is not without standard error. In general, the error in the coordinates tends to be reduced as the resolution is increased, since more
15 experimental diffraction data is available for the model fitting and refinement. Thus, for example, more diffraction data can be collected from a crystal that diffracts to a resolution of 2.8 angstroms than from a crystal that diffracts to a lower resolution, such as 3.5 angstroms. Consequently, the refined structural coordinates will usually be more accurate when fitted and refined using data from
20 a crystal that diffracts to higher resolution. The design of ligands and modulators for GR or any other NR depends on the accuracy of the structural coordinates. If the coordinates are not sufficiently accurate, then the design process will be ineffective. In most cases, it is very difficult or impossible to collect sufficient diffraction data to define atomic coordinates precisely when the crystals diffract to
25 a resolution of only 3.5 angstroms or poorer. Thus, in most cases, it is difficult to use X-ray structures in structure-based ligand design when the X-ray structures are based on crystals that diffract to a resolution of only 3.5 angstroms or poorer. However, common experience has shown that crystals diffracting to 2.8 angstroms or better can yield X-ray structures with sufficient accuracy to greatly
30 facilitate structure-based drug design. Further improvement in the resolution can further facilitate structure-based design, but the coordinates obtained at 2.8 angstroms resolution are generally adequate for most purposes.

Also, those of skill in the art will understand that NR proteins can adopt

different conformations when different ligands are bound. In particular, NR proteins will adopt substantially different conformations when agonists and antagonists are bound. Subtle variations in the conformation can also occur when different agonists are bound, and when different antagonists are bound. These variations can be difficult or impossible to predict from a single X-ray structure. Generally, structure-based design of GR modulators depends to some degree on a knowledge of the differences in conformation that occur when agonists and antagonists are bound. Thus, structure-based modulator design is most facilitated by the availability of X-ray structures of complexes with potent agonists as well as potent antagonists.

As used herein, the term "substantially pure" means that the polynucleotide or polypeptide is substantially free of the sequences and molecules with which it is associated in its natural state, and those molecules used in the isolation procedure. The term "substantially free" means that the sample is at least 50%, preferably at least 70%, more preferably 80% and most preferably 90% free of the materials and compounds with which it is associated in nature.

As used herein, the term "target cell" refers to a cell, into which it is desired to insert a nucleic acid sequence or polypeptide, or to otherwise effect a modification from conditions known to be standard in the unmodified cell. A nucleic acid sequence introduced into a target cell can be of variable length. Additionally, a nucleic acid sequence can enter a target cell as a component of a plasmid or other vector or as a naked sequence.

As used herein, the term "transcription" means a cellular process involving the interaction of an RNA polymerase with a gene that directs the expression as RNA of the structural information present in the coding sequences of the gene. The process includes, but is not limited to the following steps: (a) the transcription initiation, (b) transcript elongation, (c) transcript splicing, (d) transcript capping, (e) transcript termination, (f) transcript polyadenylation, (g) nuclear export of the transcript, (h) transcript editing, and (i) stabilizing the transcript.

As used herein, the term "transcription factor" means a cytoplasmic or nuclear protein which binds to such gene, or binds to an RNA transcript of such gene, or binds to another protein which binds to such gene or such RNA transcript or another protein which in turn binds to such gene or such RNA transcript, so as

to thereby modulate expression of the gene. Such modulation can additionally be achieved by other mechanisms; the essence of "transcription factor for a gene" is that the level of transcription of the gene is altered in some way.

As used herein, the term "unit cell" means a basic parallelipiped shaped block. The entire volume of a crystal can be constructed by regular assembly of such blocks. Each unit cell comprises a complete representation of the unit of pattern, the repetition of which builds up the crystal. Thus, the term "unit cell" means the fundamental portion of a crystal structure that is repeated infinitely by translation in three dimensions. A unit cell is characterized by three vectors a, b, and c, not located in one plane, which form the edges of a parallelepiped. Angles α , β and γ define the angles between the vectors: angle α is the angle between vectors b and c; angle β is the angle between vectors a and c; and angle γ is the angle between vectors a and b. The entire volume of a crystal can be constructed by regular assembly of unit cells; each unit cell comprises a complete representation of the unit of pattern, the repetition of which builds up the crystal.

II. Description of Tables

Table 1 is chart of sequence identity between the ligand binding domains of several nuclear receptors.

Table 2 is a table listing mutations of the GR LBD (521-777) gene for testing solution solubility and stability. SEQ ID NOs:7-8 and 15-16 also comprise these mutations. Candidate mutated residues include but are not limited to Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

Table 2A is a table listing mutations that were discovered using the LacI-based "peptides-on-plasmids" technique with GR LBD.

Table 3 is a table summarizing the crystal and data statistics obtained from the crystallized ligand binding domain of GR α LBD that was co-crystallized with dexamethasone and a fragment of the co-activator TIF2. Data on the unit cell are presented, including data on the crystal space group, unit cell dimensions, molecules per asymmetric cell and crystal resolution.

Table 4 is a table of the atomic structure coordinate data obtained from X-ray diffraction from the ligand binding domain of GR (residues 521-777) in complex with desamethasone and a fragment of the co-activator TIF2.

Table 5 is a table of the atomic structure coordinates used as the initial model to solve the structure of the GR/TIF2/dexamethasone complex by molecular replacement. The GR model is a homology model built on the published structure of the progesterone receptor LBD and the SRC1 coactivator peptide from the PPAR α /Compound 1/SRC1 structure.

III. General Considerations

The present invention will usually be applicable *mutatis mutandis* to nuclear receptors in general, more particularly to steroid receptors and even more particularly to glucocorticoid receptors, including GR isoforms, as discussed herein, based, in part, on the patterns of nuclear receptor and steroid receptor structure and modulation that have emerged as a consequence of the present disclosure, which in part discloses determining the three dimensional structure of the ligand binding domain of GR α in complex with dexamethasone and a fragment of the co-activator TIF2.

The nuclear receptor superfamily has been subdivided into two subfamilies: the GR subfamily (also referred to as the steroid receptors and denoted SRs), comprising GR, AR (androgen receptor), MR (mineralcorticoid receptor) and PR (progesterone receptor) and the thyroid hormone receptor (TR) subfamily, comprising TR, vitamin D receptor (VDR), retinoic acid receptor (RAR), retinoid X receptor (RXR), and most orphan receptors. This division has been made on the basis of DNA binding domain structures, interactions with heat shock proteins (HSP), and ability to form dimers.

Steroid receptors (SRs) form a subset of the superfamily of nuclear receptors. The glucocorticoid receptor is a steroid receptor and thus a member of the superfamily of nuclear receptors and the subset of steroid receptors. The human glucocorticoid receptor exists in two isoforms, GR α which consists of 777 amino acids and GR β which consists of 742 amino acids. As noted, the alpha isoform of human glucocorticoid receptor is made up of 777 amino acids and is predominantly cytoplasmic in its unactivated, non-DNA binding form. When activated, it translocates to the nucleus. In order to understand the role played by the glucocorticoid receptor in the different cell processes, the receptor was mapped by transfecting receptor-negative and glucocorticoid-resistant cells with

different steroid receptor constructs and reporter genes like chloramphenicol acyltransferase (CAT) or luciferase which had been covalently linked to a glucocorticoid responsive element (GRE). From these and other studies, four major functional domains have become evident.

5 From amino to carboxyl terminal end, these functional domains include the tau 1, DNA binding, and ligand binding domains in succession. The tau 1 domain spans amino acid positions 77-262 and regulates gene activation. The DNA binding domain is from amino acid positions 421-486 and has nine cysteine residues, eight of which are organized in the form of two zinc fingers analogous to
10 *Xenopus* transcription factor IIIA. The DNA binding domain binds to the regulatory sequences of genes that are induced or deinduced by glucocorticoids. Amino acids 521 to 777 form the ligand binding domain, which binds glucocorticoid to activate the receptor. This region of the receptor also has the nuclear localization signal. Deletion of this carboxyl terminal end results in a receptor that is
15 constitutively active for gene induction (up to 30% of wild type activity) and even more active for cell kill (up to 150% of wild type activity) (Giguere et al., (1986) *Cell* 46: 645-652; Hollenberg et al., (1987) *Cell* 49: 39-46; Hollenberg & Evans, (1988) *Cell* 55: 899-906; Hollenberg et al., (1989) *Cancer Res.* 49: 2292s-2294s; Oro et al., (1988) *Cell* 55: 1109-1114; Evans, (1989) in Recent Progress in
20 Hormone Research (Clark, ed.) Vol. 45, pp. 1-27, Academic Press, San Diego, California; Green & Chambon, (1987) *Nature* 325: 75-78; Picard & Yamamoto, (1987) *EMBO J.* 6: 3333-3340; Picard et al., (1990) *Cell Regul.* 1: 291-299; Godowski et al., (1987) *Nature* 325: 365-368; Miesfeld et al., (1987) *Science* 236:423-427; Danielsen et al., (1989) *Cancer Res.* 49: 2286s-2291s; Danielsen et
25 al., (1987) *Molec. Endocrinol.* 1: 816-822; Umesono & Evans, (1989) *Cell* 57: 1139-1146.). Despite the aforementioned indirect characterization of the structure of GR α , until the present disclosure, a detailed three-dimensional model of the ligand binding domain of GR α has not been achieved.

GR subgroup members are tightly bound by heat shock protein(s) (HSP) in
30 the absence of ligand, dimerize following ligand binding and dissociation of HSP, and show homology in the DNA half sites to which they bind. These half sites also tend to be arranged as palindromes. TR subgroup members tend to be bound to DNA or other chromatin molecules when unliganded, can bind to DNA

as monomers and dimers, but tend to form heterodimers, and bind DNA elements with a variety of orientations and spacings of the half sites, and also show homology with respect to the nucleotide sequences of the half sites. ER does not belong to either subfamily, since it resembles the GR subfamily in hsp
5 interactions, and the TR subfamily in nuclear localization and DNA-binding properties.

Most members of the superfamily, including orphan receptors, possess at least two transcription activation subdomains, one of which is constitutive and resides in the amino terminal domain (AF-1), and the other of which (AF-2)
10 resides in the ligand binding domain, whose activity is regulated by binding of an agonist ligand. The function of AF-2 requires an activation domain (also called transactivation domain) that is highly conserved among the receptor superfamily. Most LBDs contain an activation domain. Some mutations in this domain abolish AF-2 function, but leave ligand binding and other functions unaffected. Ligand
15 binding allows the activation domain to serve as an interaction site for essential co-activator proteins that function to stimulate (or in some cases, inhibit) transcription.

Analysis and alignment of amino acid sequences, and X-ray and NMR structure determinations, have shown that nuclear receptors have a modular
20 architecture with three main domains:

- 1) a variable amino-terminal domain;
- 2) a highly conserved DNA-binding domain (DBD); and
- 3) a less conserved carboxy-terminal ligand binding domain (LBD).

In addition, nuclear receptors can have linker segments of variable length
25 between these major domains. Sequence analysis and X-ray crystallography, including the disclosure of the present invention, have confirmed that GR also has the same general modular architecture, with the same three domains. The function of GR in human cells presumably requires all three domains in a single amino acid sequence. However, the modularity of GR permits different domains
30 of each protein to separately accomplish certain functions. Some of the functions of a domain within the full-length receptor are preserved when that particular domain is isolated from the remainder of the protein. Using conventional protein chemistry techniques, a modular domain can sometimes be separated from the

parent protein. Using conventional molecular biology techniques, each domain can usually be separately expressed with its original function intact or, as discussed herein below, chimeras comprising two different proteins can be constructed, wherein the chimeras retain the properties of the individual functional domains of the respective nuclear receptors from which the chimeras were generated.

The carboxy-terminal activation subdomain, is in close three dimensional proximity in the LBD to the ligand, so as to allow for ligands bound to the LBD to coordinate (or interact) with amino acid(s) in the activation subdomain. As described herein, the LBD of a nuclear receptor can be expressed, crystallized, its three dimensional structure determined with a ligand bound (either using crystal data from the same receptor or a different receptor or a combination thereof), and computational methods used to design ligands to its LBD, particularly ligands that contain an extension moiety that coordinates the activation domain of the nuclear receptor.

The LBD is the second most highly conserved domain in these receptors. As its name suggests, the LBD binds ligands. With many nuclear receptors, including GR, binding of the ligand can induce a conformational change in the LBD that can, in turn, activate transcription of certain target genes. Whereas integrity of several different LBD sub-domains is important for ligand binding, truncated molecules containing only the LBD retain normal ligand-binding activity. This domain also participates in other functions, including dimerization, nuclear translocation and transcriptional activation, as described herein.

Nuclear receptors usually have HSP binding domains that present a region for binding to the LBD and can be modulated by the binding of a ligand to the LBD. For many of the nuclear receptors ligand binding induces a dissociation of heat shock proteins such that the receptors can form dimers in most cases, after which the receptors bind to DNA and regulate transcription. Consequently, a ligand that stabilizes the binding or contact of the heat shock protein binding domain with the LBD can be designed using the computational methods described herein.

With the receptors that are associated with the HSP in the absence of the ligand, dissociation of the HSP results in dimerization of the receptors.

Dimerization is due to receptor domains in both the DBD and the LBD. Although the main stimulus for dimerization is dissociation of the HSP, the ligand-induced conformational changes in the receptors can have an additional facilitative influence. With the receptors that are not associated with HSP in the absence of the ligand, particularly with the TR, ligand binding can affect the pattern of dimerization. The influence depends on the DNA binding site context, and can also depend on the promoter context with respect to other proteins that can interact with the receptors. A common pattern is to discourage monomer formation, with a resulting preference for heterodimer formation over dimer formation on DNA.

Nuclear receptor LBDs usually have dimerization domains that present a region for binding to another nuclear receptor and can be modulated by the binding of a ligand to the LBD. Consequently, a ligand that disrupts the binding or contact of the dimerization domain can be designed using the computational methods described herein to produce a partial agonist or antagonist.

The amino terminal domain of GR is the least conserved of the three domains. This domain is involved in transcriptional activation and, its uniqueness might dictate selective receptor-DNA binding and activation of target genes by GR subtypes. This domain can display synergistic and antagonistic interactions with the domains of the LBD.

The DNA binding domain has the most highly conserved amino acid sequence amongst the GRs. It typically comprises about 70 amino acids that fold into two zinc finger motifs, wherein a zinc atom coordinates four cysteines. The DBD comprises two perpendicularly oriented α -helices that extend from the base of the first and second zinc fingers. The two zinc fingers function in concert along with non-zinc finger residues to direct the GR to specific target sites on DNA and to align receptor dimer interfaces. Various amino acids in the DBD influence spacing between two half-sites (which usually comprises six nucleotides) for receptor dimerization. The optimal spacings facilitate cooperative interactions between DBDs, and D box residues are part of the dimerization interface. Other regions of the DBD facilitate DNA-protein and protein-protein interactions are involved in dimerization.

In nuclear receptors that bind to a HSP, the ligand-induced dissociation of HSP with consequent dimer formation allows, and therefore, promotes DNA binding. With receptors that are not associated (as in the absence of ligand), ligand binding tends to stimulate DNA binding of heterodimers and dimers, and to discourage monomer binding to DNA. However, with DNA containing only a single half site, the ligand tends to stimulate the receptor's binding to DNA. The effects are modest and depend on the nature of the DNA site and probably on the presence of other proteins that can interact with the receptors. Nuclear receptors usually have DBD (DNA binding domains) that present a region for binding to DNA and this binding can be modulated by the binding of a ligand to the LBD.

The modularity of the members of the nuclear receptor superfamily permits different domains of each protein to separately accomplish different functions, although the domains can influence each other. The separate function of a domain is usually preserved when a particular domain is isolated from the remainder of the protein. Using conventional protein chemistry techniques a modular domain can sometimes be separated from the parent protein. By employing conventional molecular biology techniques each domain can usually be separately expressed with its original function intact or chimerics of two different nuclear receptors can be constructed, wherein the chimerics retain the properties of the individual functional domains of the respective nuclear receptors from which the chimerics were generated.

Various structures have indicated that most nuclear receptor LBDs adopt the same general folding pattern. This fold consists of 10-12 alpha helices arranged in a bundle, together with several beta-strands, and linking segments. A preferred GR α LBD structure of the present invention has 10-11 helices, depending on whether helix-3' is counted. Structural studies have shown that most of the alpha-helices and beta-strands have the same general position and orientation in all nuclear receptor structures, whether ligand is bound or not. However, the AF2 helix has been found in different positions and orientations relative to the main bundle, depending on the presence or absence of the ligand, and also on the chemical nature of the ligand. These structural studies have suggested that many nuclear receptors share a common mechanism of activation, where binding of activating ligands helps to stabilize the AF2 helix in a position

and orientation adjacent to helices-3, -4, and -10, covering an opening to the ligand binding site. This position and orientation of the AF2 helix, which will be called the "active conformation", creates a binding site for co-activators. See, e.g., Nolte et al., (1998) *Nature* 395:137-43; Shiau et al., (1998) *Cell* 95: 927-37. This

5 co-activator binding site has a central lipophilic pocket that can accommodate leucine side-chains from co-activators, as well as a "charge-clamp" structure consisting essentially of a lysine residue from helix-3 and a glutamic acid residue from the AF2 helix.

Structural studies have shown that co-activator peptides containing the

10 sequence LXXLL (where L is leucine and X can be a different amino acid in different cases) can bind to this co-activator binding site by making interactions with the charge clamp lysine and glutamic acid residues, as well as the central lipophilic region. This co-activator binding site is disrupted when the AF2 helix is shifted into other positions and orientations. In PPAR γ , activating ligands such as

15 rosiglitazone (BRL49653) make a hydrogen bonding interaction with tyrosine-473 in the AF2 helix. Nolte et al., (1998) *Nature* 395:137-43; Gampe et al., (2000) *Mol. Cell* 5: 545-55. Similarly, in GR, the dexamethasone ligand makes van der Waals interaction with the side chain of leucine-753 from the AF2 helix. This interaction is believed in part to stabilize the AF2 helix in the active conformation,

20 thereby allowing co-activators to bind and thus activating transcription from target genes.

With certain antagonist ligands, or in the absence of any ligand, the AF2 helix can be held less tightly in the active conformation, or can be free to adopt other conformations. This would either destabilize or disrupt the co-activator

25 binding site, thereby reducing or eliminating co-activator binding and transcription from certain target genes. Some of the functions of the GR protein depend on having the full-length amino acid sequence and certain partner molecules, such as co-activators and DNA. However, other functions, including ligand binding and ligand-dependent conformational changes, can be observed experimentally using

30 isolated domains, chimeras and mutant molecules.

As described herein, the LBD of a GR can be mutated or engineered, expressed, crystallized, its three dimensional structure determined with a ligand bound as disclosed in the present invention, and computational methods can be

used to design ligands to nuclear receptors, preferably to steroid receptors, and more preferably to glucocorticoid receptors.

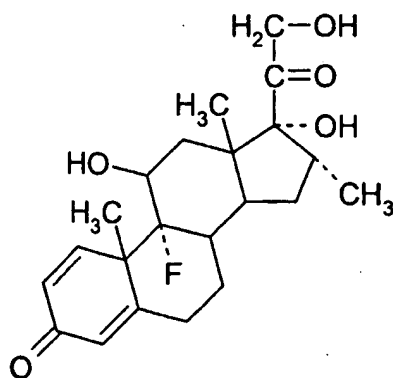
IV. The Dexamethasone Ligand

5 Ligand binding can induce transcriptional activation functions in a variety of ways. One way is through the dissociation of the HSP from receptors. This dissociation, with consequent dimerization of the receptors and their binding to DNA or other proteins in the nuclear chromatin, allows transcriptional regulatory properties of the receptors to be manifest. This can be especially true of such
10 functions on the amino terminus of the receptors.

Another way is to alter the receptor to interact with other proteins involved in transcription. These could be proteins that interact directly or indirectly with elements of the proximal promoter or proteins of the proximal promoter. Alternatively, the interactions can be through other transcription factors that
15 themselves interact directly or indirectly with proteins of the proximal promoter. Several different proteins have been described that bind to the receptors in a ligand-dependent manner. In addition, it is possible that in some cases, the ligand-induced conformational changes do not affect the binding of other proteins to the receptor, but do affect their abilities to regulate transcription.

20 In one aspect of the present invention, a GR LBD was co-crystallized with a fragment of the co-activator TIF2 and the ligand dexamethasone. Dexamethasone is a synthetic adrenocortical steroid with a molecular weight of 392.47. The IUPAC name for dexamethasone is (11 β , 16 α)-9-fluoro-11 β ,17,21-trihydroxy-16 α -methylpregna-1-4-diene-3,20-dione. The empirical formula for
25 dexamethasone is C₂₂H₂₉FO₅. Dexamethasone is represented by the chemical structure:

-42-



Dexamethasone-based therapeutics are commercially available in a variety of forms and formulations. Dexamethasone can also be purchased from various suppliers such as Sigma (St. Louis Missouri), as well as starting materials for the synthesis of dexamethasone. The synthesis of dexamethasone, and dexamethasone derivatives, is known and described in a variety of sources, including Arth et al., (1958) *J. Am. Chem. Soc.* 80: 3161; Oliveto et al., (1958) *J. Am. Chem. Soc.* 4431, Fried & Sabo, (1954) *J. Am. Chem. Soc.* 76: 1455; Hirschman et al., (1956) *J. Am. Chem. Soc.* 78: 4957 and U.S. Patent No. 3,007,923 to Muller et al., all of which are incorporated herein in their entirety.

V. The TIF2 Fragment

The nuclear receptor co-activator TIF2 (SEQ ID NO:17) was co-crystallized in one aspect of the present invention. Structurally, the nuclear receptor coactivator TIF2 comprises one domain that reacts with a nuclear receptor (nuclear receptor interaction domain, abbreviated "NID") and two autonomous activation domains, AD1 and AD2 (Voegel et al., (1998) *EMBO J.* 17: 507-519). The TIF2 NID comprises three NR-interacting modules, with each module comprising the motif, LXXLL (SEQ ID NO:18) (Voegel et al., (1998) *EMBO J.* 17: 507-519). Mutation of the motif abrogates TIF2's ability to interact with the ligand-induced activation function-2 (AF-2) found in the ligand-binding domains (LBDs) of many NRs. Presently, it is thought that TIF2 AD1 activity is mediated by CREB binding protein (CBP), however, TIF2 AD2 activity does not appear to involve interaction with CBP (Voegel et al., (1998) *EMBO J.* 17: 507-519).

In the present invention, residues 732-756 of the TIF2 protein (SEQ ID NO:17) were co-crystallized with GR and dexamethasone. These residues comprise the LXXLL (SEQ ID NO:18) of AD-2, the third motif in the linear sequence of TIF2. The TIF2 fragment is 25 residues in length and was synthesized using an automated peptide synthesis apparatus. SEQ ID NO:17, and other sequences corresponding to TIF2 and other co-activators and co-repressors, can be similarly synthesized using automated apparatuses.

VI. Production of NR, SR and GR Polypeptides

In a preferred embodiment, the present invention provides for the first time for the expression of a soluble GR polypeptide in bacteria, more preferably, in *E. coli*. The GR polypeptides of the present invention, disclosed herein, can thus now provide a variety of host-expression vector systems to express an NR, SR or GR coding sequence. These include but are not limited to microorganisms such as bacteria transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing an NR, SR or GR coding sequence; yeast transformed with recombinant yeast expression vectors containing an NR, SR or GR coding sequence; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing an NR, SR or GR coding sequence; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing an NR, SR or GR coding sequence; or animal cell systems. The expression elements of these systems vary in their strength and specificities. Methods for constructing expression vectors that comprise a partial or the entire native or mutated NR and GR polypeptide coding sequence and appropriate transcriptional/translational control signals include *in vitro* recombinant DNA techniques, synthetic techniques and *in vivo* recombination/genetic recombination. See, for example, the techniques described throughout Sambrook et al., (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York, and Ausubel et al., (1989) Current Protocols in Molecular Biology, Greene Publishing Associates and Wiley Interscience, New York, both incorporated herein in their entirety.

Depending on the host/vector system utilized, any of a number of suitable transcription and translation elements, including constitutive and inducible promoters, can be used in the expression vector. For example, when cloning in bacterial systems, inducible promoters such as pL of bacteriophage λ , plac, ptrp, ptac (ptrp-lac hybrid promoter) and the like can be used. When cloning in insect cell systems, promoters such as the baculovirus polyhedrin promoter can be used. When cloning in plant cell systems, promoters derived from the genome of plant cells, such as heat shock promoters; the promoter for the small subunit of RUBISCO; the promoter for the chlorophyll a/b binding protein) or from plant viruses (e.g., the 35S RNA promoter of CaMV; the coat protein promoter of TMV) can be used. When cloning in mammalian cell systems, promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter) can be used. When generating cell lines that contain multiple copies of the tyrosine kinase domain DNA, SV40-, BPV- and EBV-based vectors can be used with an appropriate selectable marker.

Adequate levels of expression of nuclear receptor LBDs can be obtained by the novel approaches described herein. High level expression in *E. coli* of ligand binding domains of TR and other nuclear receptors, including members of the steroid/thyroid receptor superfamily, such as the estrogen (ER), androgen (AR), mineralocorticoid (MR), progesterone (PR), RAR, RXR and vitamin D (VDR) receptors can also be achieved after review of the expression of a soluble GR polypeptide in bacteria, more preferably, *E. coli* disclosed herein. The GR polypeptides of the present invention, disclosed herein, can thus now provide a variety of host-expression vector systems. Yeast and other eukaryotic expression systems can be used with nuclear receptors that bind heat shock proteins since these nuclear receptors are generally more difficult to express in bacteria, with the exception of ER, which can be expressed in bacteria. In a preferred embodiment of the present invention, as disclosed in the Examples, a GR LBD is expressed in *E. coli*.

Representative nuclear receptors or their ligand binding domains have been cloned and sequenced, including human RAR α , human RAR γ , human RXR α , human RXR β , human PPAR α , human PPAR β or δ (delta), human PPAR γ ,

human VDR, human ER (as described in Seielstad et al., (1995) *Mol. Endocrinol.* 9: 647-658), human GR, human PR, human MR, and human AR. The ligand binding domain of each of these nuclear receptors has been identified. Using this information in conjunction with the methods described herein, one of ordinary skill
5 in the art can express and purify LBDs of any of the nuclear receptors, bind it to an appropriate ligand, and crystallize the nuclear receptor's LBD with a bound ligand, if desired.

Extracts of expressing cells are a suitable source of receptor for purification and preparation of crystals of the chosen receptor. To obtain such expression, a
10 vector can be constructed in a manner similar to that employed for expression of the rat TR alpha (Apriletti et al., (1995) *Protein Expression and Purification*, 6: 368-370). The nucleotides encoding the amino acids encompassing the ligand binding domain of the receptor to be expressed can be inserted into an expression vector such as the one employed by Apriletti et al (1995). Stretches of adjacent
15 amino acid sequences can be included if more structural information is desired.

The native and mutated nuclear receptors in general, and more particularly SR and GR polypeptides, and fragments thereof, of the present invention can also be chemically synthesized in whole or part using techniques that are known in the art (See, e.g., Creighton, (1983) Proteins: Structures and Molecular Principles,
20 W.H. Freeman & Co., New York, incorporated herein in its entirety).

In a preferred embodiment, the present invention provides for the first time for the expression of a soluble GR polypeptide in bacteria, more preferably, *E. coli*, and subsequent purification thereof. Representative purification techniques are also disclosed in the Examples, particularly Example 1. The GR polypeptides
25 of the present invention, disclosed herein, can thus now provide the ability to employ additional purification techniques for both liganded and unliganded NRs. Thus, it is envisioned, based upon the disclosure of the present invention, that purification of the unliganded or liganded NR, SR or GR receptor can be obtained by conventional techniques, such as hydrophobic interaction chromatography
30 (HPLC), ion exchange chromatography (HPLC), and heparin affinity chromatography. To achieve higher purification for improved crystals of nuclear receptors it is sometimes preferable to ligand shift purify the nuclear receptor using a column that separates the receptor according to charge, such as an ion

exchange or hydrophobic interaction column, and then bind the eluted receptor with a ligand. The ligand induces a change in the receptor's surface charge such that when re-chromatographed on the same column, the receptor then elutes at the position of the liganded receptor and is removed by the original column run with the unliganded receptor. Typically, saturating concentrations of ligand can be used in the column and the protein can be preincubated with the ligand prior to passing it over the column.

More recently developed methods involve engineering a "tag" such as with histidine placed on the end of the protein, such as on the amino terminus, and then using a nickel chelation column for purification. See Janknecht, (1991) *Proc. Natl. Acad. Sci. U.S.A.* 88: 8972-8976 (1991), incorporated by reference.

VII. Formation of NR, SR and GR Ligand Binding Domain Crystals

In one embodiment, the present invention provides crystals of GR α LBD. The crystals were obtained using the methodology disclosed in the Laboratory Examples. The GR α LBD crystals, which can be native crystals, derivative crystals or co-crystals, have hexagonal unit cells (a hexagonal unit cell is a unit cell wherein $a = b \neq c$, and wherein $\alpha = \beta = 90^\circ$, and $\gamma = 120^\circ$) and space group symmetry P6₁. There are two GR α LBD molecule in the asymmetric unit. In this GR α crystalline form, the unit cell has dimensions of $a = b = 126.014 \text{ \AA}$, $c = 86.312 \text{ \AA}$, and $\alpha = \beta = 90^\circ$, and $\gamma = 120^\circ$. This crystal form can be formed in a crystallization reservoir as described in the Examples.

VII.A. Preparation of NR, SR and GR Crystals

The native and derivative co-crystals, and fragments thereof, disclosed in the present invention can be obtained by a variety of techniques, including batch, liquid bridge, dialysis, vapor diffusion and hanging drop methods (See, e.g., McPherson, (1982) *Preparation and Analysis of Protein Crystals*, John Wiley, New York; McPherson, (1990) *Eur. J. Biochem.* 189:1-23; Weber, (1991) *Adv. Protein Chem.* 41:1-36). In a preferred embodiment, the vapor diffusion and hanging drop methods are used for the crystallization of NR, SR and GR polypeptides and fragments thereof. A more preferred hanging drop method technique is disclosed in the Examples.

In general, native crystals of the present invention are grown by dissolving substantially pure NR, SR or GR polypeptide or a fragment thereof in an aqueous buffer containing a precipitant at a concentration just below that necessary to precipitate the protein. Water is removed by controlled evaporation to produce precipitating conditions, which are maintained until crystal growth ceases.

In one embodiment of the invention, native crystals are grown by vapor diffusion (See, e.g., McPherson, (1982) Preparation and Analysis of Protein Crystals, John Wiley, New York.; McPherson, (1990) *Eur. J. Biochem.* 189:1-23). In this method, the polypeptide/precipitant solution is allowed to equilibrate in a closed container with a larger aqueous reservoir having a precipitant concentration optimal for producing crystals. Generally, less than about 25 μ L of NR, SR or GR polypeptide solution is mixed with an equal volume of reservoir solution, giving a precipitant concentration about half that required for crystallization. This solution is suspended as a droplet underneath a coverslip, which is sealed onto the top of the reservoir. The sealed container is allowed to stand, until crystals grow. Crystals generally form within two to six weeks, and are suitable for data collection within approximately seven to ten weeks. Of course, those of skill in the art will recognize that the above-described crystallization procedures and conditions can be varied.

VII.B. Preparation of Derivative Crystals

Derivative crystals of the present invention, e.g. heavy atom derivative crystals, can be obtained by soaking native crystals in mother liquor containing salts of heavy metal atoms. Such derivative crystals are useful for phase analysis in the solution of crystals of the present invention. In a preferred embodiment of the present invention, for example, soaking a native crystal in a solution containing methyl-mercury chloride provides derivative crystals suitable for use as isomorphous replacements in determining the X-ray crystal structure of a NR, SR or GR polypeptide. Additional reagents useful for the preparation of the derivative crystals of the present invention will be apparent to those of skill in the art after review of the disclosure of the present invention presented herein.

VII.C. Preparation of Co-crystals

Co-crystals of the present invention can be obtained by soaking a native crystal in mother liquor containing compounds known or predicted to bind the LBD of a NR, SR or GR, or a fragment thereof. Alternatively, co-crystals can be obtained by co-crystallizing a NR, SR or GR LBD polypeptide or a fragment thereof in the presence of one or more compounds known or predicted to bind the polypeptide. In a preferred embodiment, as disclosed in the Examples, such a compound is dexamethasone.

VII.D. Solving a Crystal Structure of the Present Invention

Crystal structures of the present invention can be solved using a variety of techniques including, but not limited to, isomorphous replacement, anomalous scattering or molecular replacement methods. Computer software packages are also helpful in solving a crystal structure of the present invention. Applicable software packages include but are not limited to the CCP4 package disclosed in the Examples, the X-PLOR™ program (Brünger, (1992) *X-PLOR, Version 3.1. A System for X-ray Crystallography and NMR*, Yale University Press, New Haven, Connecticut; X-PLOR is available from Molecular Simulations, Inc., San Diego, California), Xtal View (McRee, (1992) *J. Mol. Graphics* 10: 44-46; X-tal View is available from the San Diego Supercomputer Center). SHELXS 97 (Sheldrick (1990) *Acta Cryst.* A46: 467; SHELX 97 is available from the Institute of Inorganic Chemistry, Georg-August-Universität, Göttingen, Germany), HEAVY (Terwilliger, Los Alamos National Laboratory) and SHAKE-AND-BAKE (Hauptman, (1997) *Curr. Opin. Struct. Biol.* 7: 672-80; Weeks et al., (1993) *Acta Cryst.* D49: 179; available from the Hauptman-Woodward Medical Research Institute, Buffalo, New York) can be used. See also, Ducruix & Geige, (1992) *Crystallization of Nucleic Acids and Proteins: A Practical Approach*, IRL Press, Oxford, England, and references cited therein.

VIII. Characterization and Solution of a GR α Ligand Binding Domain Crystal

Referring now to Figure 3A, the overall arrangement of the GR LBD dimer is depicted in a ribbon/worm diagram that was derived from the crystalline polypeptide of the present invention. The two GR LBDs are shown in white and

gray worm representation. The TIF2 peptides **TIF2** are shown in gray ribbon and two dexamethasone ligands **DEX** are shown in space filling. The N terminus and C terminus of each GR LBD are labeled with a **C** and **N**, respectively. There is an interface between the two LBDs at beta turns and beta strands.

5 Referring now to Figures 3B and 3C, two orientations of the GR/TIF2/DEX complex are depicted. In each figure, the TIF2 peptide **TIF2** is shown in ribbon and the GR LBD is shown in worm. The AF2 helix **AF2** of GR is shown in gray worm in each figure. The key structural elements helix 9 **H9** and helix 3 **H3** are indicated, as is the N terminus **N**. The DEX compound **DEX** is shown in dark gray shading. In Figures 3B and 3C, the interaction of helix 3 **H3** and the AF2 helix **AF2** with dexamethasone **DEX** can be seen.

10 Referring now to Figures 4A and 4B, the overlap of GR LBD with the LBDs of the AR and PR (Figures 4A and 4B, respectively) is depicted. The AR and PR are shown as a thin line, while the GR is shown as a thick line. Backbone Calpha atoms are also shown. This superposition is consistent with the sequence alignment approach taken in the design of the GR LBD polypeptide disclosed herein.

RMS deviation calculation results were as follows:

20		GR	PR	AR
	GR	0.00	0.94	1.56
	PR	0.94	0.00	1.34
	AR	1.56	1.34	0.00

25 where in each of the three calculations, the RMS deviation was computed using 980 N, backbone C alpha, C, O atoms from 245 aligned residues. These 245 residues are GR:531-775, PR:686-987,899-931 and AR:672-883,885-917. Several GR and PR residues before helix-1 were omitted in the calculations, as was one residue at the C-terminus, to correspond to the shorter AR construct.

30 One residue (PR:898 and AR:884) was also omitted in the 10-AF2 loop because of the deletion in GR. The RMS deviations suggest that the AR structure has diverged away from GR and PR, and graphical examination confirmed this at least qualitatively.

Referring now to Figure 5, a sequence alignment of steroid receptors, particularly an alignment of the F602S GR α sequence with MR, PR, AR, ER α , and ER β is depicted. Residues that lie within 5.0 angstroms of the ligand are identified with small square boxes around the one-letter amino acid code. The ligands used for this calculation are dexamethasone (for GR), progesterone (for PR), dihydrotestosterone (for AR), estradiol (for ER α) and genistein (for ER β). The alpha-helices and beta-strands observed in the X-ray structures are identified by the larger boxes and captions. Note that the secondary structure of MR is not publicly known at this time, and is thus not annotated in the Figure. More than one structure is available for PR, AR, ER α and ER β , and, in some cases, the alpha-helices have different endpoints in these different X-ray structures. The variation in the alpha-helices is indicated here by using boxes with thicker and thinner linewidths, where the thicker linewidth box encompasses residues that adopt the same secondary structure in all available X-ray structures, and thinner linewidth boxes encompass residues that adopt an alpha-helical structure in some but not all X-ray structures. The secondary structures were determined by graphical examination of the X-ray structures.

It is also noted that, within the ligand binding domains (LBDs), the sequence identity is as follows:

20

Table 1
Sequence Identity of NR LBDs

	GR	MR	PR	AR
GR	100%	56%	54%	50%
25 MR	56%	100%	55%	51%
PR	54%	55%	100%	55%
AR	50%	51%	55%	100%

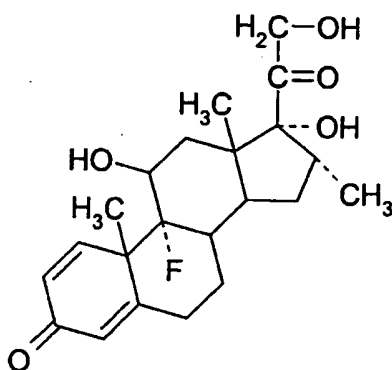
VIII.A Unique Structural Differences Between GR α and Other SRs

Even though the GR LBD shares over 50% sequence identity with PR and AR and fold into a similar three-layer helical sandwich (Figure 4A and 4B), there are a number of unique structural differences in their structures. The most distinct differences are noted in the extended strand between helices 1 and 3, and the

position of helix 7. These differences contribute a unique shape of the binding pocket for each receptor (Figures 6A and 6B) and may thus provide a molecular basis for steroid specificity of these receptors. The detailed structural information about the GR LBD and the pocket provided herein can be further exploited to design receptor specific agonists or antagonists.

VIII.B Dexamethasone

The ligand binding domain of GR α was co-crystallized with dexamethasone, which has the IUPAC name (11 β , 16 α)-9-fluoro-11 β ,17,21-trihydroxy-16 α -methylpregna-1-4-diene-3,20-dione and is shown below.



Dexamethasone is an agonist of GR α and is useful for treatment of GR α -mediated diseases or conditions including inflammation, tissue rejection, auto-immunity, malignancies such as leukemias and lymphomas, Cushing's syndrome, acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, polyarteritis nodosa, granulomatous polyarteritis, inhibition of myeloid cell lines, immune proliferation/apoptosis, HPA axis suppression and regulation, hypercortisolemia, modulation of the Th1/Th2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hyperglycemia, acute adrenal insufficiency, chronic primary adrenal insufficiency, secondary adrenal insufficiency, congenital adrenal hyperplasia, cerebral edema, thrombocytopenia, and Little's syndrome as well as many other conditions.

VIII.C. Characterization of the GR α Binding Pocket and Interactions Between GR α and Dexamethasone

Referring now to Figure 6A, the GR ligand binding pocket is depicted schematically. The GR ligand binding pocket is shown in a worm representation and the pocket is shown with a white surface. The gross shape of the binding pocket is depicted here with a smooth surface that covers the available volume within the binding pocket. The available volume is mapped by placing the protein within a grid, and then checking, for each grid point, whether a spherical probe atom can fit at that point without bumping into the protein. The spacing of grid points was taken as 0.50Å, and the radius of the probe atom was taken as 1.40Å. Atoms in the protein were represented as spheres with a radius of 1.20Å for hydrogen, 1.70Å for carbon, 1.55Å for nitrogen, 1.52Å for oxygen and 1.80Å for sulfur. These are essentially the atomic radius values suggested by Bondi (A. Bondi, "van der Waals Volumes and Radii," Journal of Physical Chemistry, 68, 441-451 (1964)). The protein was represented with all hydrogen atoms in order to handle its volume more accurately. These hydrogen atoms were added to obtain the protonation states expected at pH 7 using the MVP program. The MVP program adds hydrogens using standard geometry, and then refines the initial coordinates with energy minimization, holding all heavy atoms fixed. The "available" grid points are defined as those for which the probe sphere does not bump into any sphere corresponding to a protein atom. The smooth surface was then constructed over these available binding site grid points using the dot surface program of Connolly (Michael L. Connolly, "Solvent-Accessible Surfaces of Proteins and Nucleic Acids," Science 221, 709-713 (1983)) with a probe radius of 1.30Å. The protein chain is shown with a backbone ribbon depiction.

Referring now to Figure 6B, electron density in the GR-dexamethasone interface is depicted. The electron density is calculated with F_o coefficient and shown in a one sigma cutoff. The ligand DEX is in the center of the figure. Key residues L732, A605, R611, Q570, G567, N564, and F749 encircle ligand DEX. Ligand DEX displays a good spatial fit, with no overlaps and no apparent charge repulsions.

Referring now to Figure 7, molecular interactions between the GR protein and the dexamethasone are depicted. There are 22 residues from GR involved in

direct interactions with the dexamethasone, and the residues are Q570, L566, G567, L563, W600, L753, N564, F749, C736, I747, M560, T739, Q642, Y735, L732, M646, M601, A605, F623, M604, L608, and R611.

5 VIII.D. Structural Mechanism of Improving Protein Solubility by the F602S Mutation

Figure 8 is a wire frame diagram that provides a closer look at the F602S mutation. The F602 is lipophilic but resides in the hydrophilic environment, a situation that could destabilize the protein. The mutation of the phenylalanine (F) to the serine (S) allows the S602 side chain to make direct hydrogen bonds with two water molecules, shown as 1H₂O and 2H₂O in Figure 8. Association distances of 2.416 and 4.036 are indicated between S602 and 1H₂O and 2H₂O, respectively. Other residues are also shown in interaction with 1H₂O and 2H₂O, and these include H726 (which is also coordinated with water molecule 1H₂O), Y764 (which is also coordinated with water molecules 1H₂O and 2H₂O), Y598 and W600. An association distance of 4.354 is shown between 1H₂O and H726; and an association distance of 3.286 is shown with Y764. An association distance of 3.157 is shown between 1H₂O and 2H₂O. It is envisioned that this complex hydrogen bond network initiated by the F602S mutation and the two water molecules improves the protein stability thus the solubility as well.

VIII.E. Generation of Easily-Solved NR, SR and GR Crystals

The present invention discloses a substantially pure GR LBD polypeptide in crystalline form. In a preferred embodiment, exemplified in the Figures and Laboratory Examples, GR α is crystallized with bound ligand. Crystals can be formed from NR, SR and GR LBD polypeptides that are usually expressed by a cell culture, such as *E. coli*. Bromo- and iodo-substitutions can be included during the preparation of crystal forms and can act as heavy atom substitutions in GR ligands and crystals of NRs, SRs and GRs. This method can be advantageous for the phasing of the crystal, which is a crucial, and sometimes limiting, step in solving the three-dimensional structure of a crystallized entity. Thus, the need for generating the heavy metal derivatives traditionally employed in crystallography can be eliminated. After the three-dimensional structure of a NR, SR or GR, or an

NR, SR or GR LBD with or without a ligand bound is determined, the resultant three-dimensional structure can be used in computational methods to design synthetic ligands for NR, SR or GR and for other NR, SR or GR polypeptides. Further activity structure relationships can be determined through routine testing, using assays disclosed herein and known in the art.

IX. Uses of NR, SR and GR Crystals and the Three-Dimensional Structure of the Ligand Binding Domain of GR α

The solved crystal structure of the present invention is useful in the design of modulators of activity mediated by the glucocorticoid receptor and by other nuclear receptors. Evaluation of the available sequence data shows that GR α is particularly similar to MR, PR and AR. The GR α LBD has approximately 55%, 54% and 50% sequence identity to the MR, PR and AR LBDs, respectively. The GR β amino acid sequence is identical to the GR α amino acid sequence for residues 1-726, but the remaining 16 residues in GR β show no significant similarity to the remaining 51 residues in GR α .

The present GR α X-ray structure can also be used to build models for targets where no X-ray structure is available, such as with GR β and MR. Indeed, a model for GR α using the available X-ray structures of PR and/or AR as templates was built and used by the present co-inventors to obtain a starting model for the molecular replacement calculation used in solving the X-ray structure of GR α disclosed herein. These models will be less accurate than X-ray structures, but can help in the design of compounds targeted for GR β and MR, for example. Also, these models can aid the design of compounds to selectively modulate any desired subset of GR α , GR β , MR, PR, AR and other related nuclear receptors.

IX.A. Design and Development of NR, SR and GR Modulators

The present invention, particularly the computational methods, can be used to design drugs for a variety of nuclear receptors, such as receptors for glucocorticoids (GRs), androgens (ARs), mineralocorticoids (MRs), progestins (PRs), estrogens (ERs), thyroid hormones (TRs), vitamin D (VDRs), retinoid (RARs and RXRs) and peroxisomal proliferators (PPARs). The present invention

can also be applied to the "orphan receptors," as they are structurally homologous in terms of modular domains and primary structure to classic nuclear receptors, such as steroid and thyroid receptors. The amino acid homologies of orphan receptors with other nuclear receptors ranges from very low (<15%) to in the
5 range of 35% when compared to rat RAR α and human TR β receptors, for example.

The knowledge of the structure of the GR α ligand binding domain (LBD), an aspect of the present invention, provides a tool for investigating the mechanism of action of GR α and other NR, SR and GR polypeptides in a subject. For
10 example, various computer modelling programs, as described herein, can predict the binding of various ligand molecules to the LBD of GR β , or another steroid receptor or, more generally, nuclear receptor. Upon discovering that such binding in fact takes place, knowledge of the protein structure then allows design and synthesis of small molecules that mimic the functional binding of the ligand to the
15 LBD of GR α , and to the LBDs of other polypeptides. This is the method of "rational" drug design, further described herein.

Use of the isolated and purified GR α crystalline structure of the present invention in rational drug design is thus provided in accordance with the present invention. Additional rational drug design techniques are described in U.S. Patent
20 Nos. 5,834,228 and 5,872,011, incorporated herein in their entirety.

Thus, in addition to the compounds described herein, other sterically similar compounds can be formulated to interact with the key structural regions of an NR, SR or GR in general, or of GR α in particular. The generation of a structural functional equivalent can be achieved by the techniques of modeling and
25 chemical design known to those of skill in the art and described herein. It will be understood that all such sterically similar constructs fall within the scope of the present invention.

IX.A.1. Rational Drug Design

30 The three-dimensional structure of ligand-binding GR α is unprecedented and will greatly aid in the development of new synthetic ligands for NR, SR and GR polypeptides, such as GR agonists and antagonists, including those that bind exclusively to any one of the GR subtypes. In addition, NRs, SRs and GRs are

well suited to modern methods, including three-dimensional structure elucidation and combinatorial chemistry, such as those disclosed in U.S. Patent Nos. 5,463,564, and 6,236,946 incorporated herein by reference. Structure determination using X-ray crystallography is possible because of the solubility
5 properties of NRs SRs and GRs. Computer programs that use crystallography data when practicing the present invention will enable the rational design of ligands to these receptors.

Programs such as RASMOL (Biomolecular Structures Group, Glaxo Wellcome Research & Development Stevenage, Hertfordshire, UK Version 2.6,
10 August 1995, Version 2.6.4, December 1998, Copyright © Roger Sayle 1992-1999) and Protein Explorer (Version 1.87, July 3, 2001, © Eric Martz, 2001 and available online at <http://www.umass.edu/microbio/chime/explorer/index.htm>) can be used with the atomic structural coordinates from crystals generated by practicing the invention or used to practice the invention by generating three-
15 dimensional models and/or determining the structures involved in ligand binding. Computer programs such as those sold under the registered trademark INSIGHT II® and the programs GRASP (Nicholls et al., (1991) *Proteins* 11: 281) and SYBYL™ (available from Tripos, Inc. of St. Louis, Missouri) allow for further manipulations and the ability to introduce new structures. In addition, high
20 throughput binding and bioactivity assays can be devised using purified recombinant protein and modern reporter gene transcription assays known to those of skill in the art in order to refine the activity of a designed ligand.

A method of identifying modulators of the activity of an NR, SR or GR polypeptide using rational drug design is thus provided in accordance with the
25 present invention. The method comprises designing a potential modulator for an NR, SR or GR polypeptide of the present invention that will form non-covalent interactions with amino acids in the ligand binding pocket based upon the crystalline structure of the GR α LBD polypeptide; synthesizing the modulator; and determining whether the potential modulator modulates the activity of the NR, SR
30 or GR polypeptide. In a preferred embodiment, the modulator is designed for an SR polypeptide. In a more preferred embodiment, the modulator is designed for a GR α polypeptide. Preferably, the GR α polypeptide comprises the amino acid sequence of any of SEQ ID NOs:2, 4, 6 and 8, and more preferably, the GR α LBD

comprises the amino acid sequence of any of SEQ ID NOs:10, 12, 14, 16 and 31. The determination of whether the modulator modulates the biological activity of an NR, SR or GR polypeptide is made in accordance with the screening methods disclosed herein, or by other screening methods known to those of skill in the art.

5 Modulators can be synthesized using techniques known to those of ordinary skill in the art.

In an alternative embodiment, a method of designing a modulator of an NR, SR or GR polypeptide in accordance with the present invention is disclosed comprising: (a) selecting a candidate NR, SR or GR ligand; (b) determining which
10 amino acid or amino acids of an NR, SR or GR polypeptide interact with the ligand using a three-dimensional model of a crystallized GR α LBD; (c) identifying in a biological assay for NR, SR or GR activity a degree to which the ligand modulates the activity of the NR, SR or GR polypeptide; (d) selecting a chemical modification of the ligand wherein the interaction between the amino acids of the NR, SR or
15 GR polypeptide and the ligand is predicted to be modulated by the chemical modification; (e) synthesizing a chemical compound with the selected chemical modification to form a modified ligand; (f) contacting the modified ligand with the NR, SR or GR polypeptide; (g) identifying in a biological assay for NR, SR or GR activity a degree to which the modified ligand modulates the biological activity of
20 the NR, SR or GR polypeptide; and (h) comparing the biological activity of the NR, SR or GR polypeptide in the presence of modified ligand with the biological activity of the NR, SR or GR polypeptide in the presence of the unmodified ligand, whereby a modulator of an NR, SR or GR polypeptide is designed.

An additional method of designing modulators of an NR, SR or GR or an
25 NR, SR or GR LBD can comprise: (a) determining which amino acid or amino acids of an NR, SR or GR LBD interacts with a first chemical moiety (at least one) of the ligand using a three dimensional model of a crystallized protein comprising an NR, SR or GR LBD in complex with a bound ligand and a co-activator; and (b) selecting one or more chemical modifications of the first chemical moiety to
30 produce a second chemical moiety with a structure to either decrease or increase an interaction between the interacting amino acid and the second chemical moiety compared to the interaction between the interacting amino acid and the first chemical moiety. This is a general strategy only, however, and variations on this

disclosed protocol would be apparent to those of skill in the art upon consideration of the present disclosure.

Once a candidate modulator is synthesized as described herein and as will be known to those of skill in the art upon contemplation of the present invention, it can be tested using assays to establish its activity as an agonist, partial agonist or antagonist, and affinity, as described herein. After such testing, a candidate modulator can be further refined by generating LBD crystals with the candidate modulator bound to the LBD. The structure of the candidate modulator can then be further refined using the chemical modification methods described herein for three dimensional models to improve the activity or affinity of the candidate modulator and make second generation modulators with improved properties, such as that of a super agonist or antagonist, as described herein.

IX.A.2. Methods for Using the GR α LBD Structural Coordinates For Molecular Design

For the first time, the present invention permits the use of molecular design techniques to design, select and synthesize chemical entities and compounds, including modulatory compounds, capable of binding to the ligand binding pocket or an accessory binding site of an NR, SR or GR and an NR, SR or GR LBD, in whole or in part. Correspondingly, the present invention also provides for the application of similar techniques in the design of modulators of any NR, SR or GR polypeptide.

In accordance with a preferred embodiment of the present invention, the structure coordinates of a crystalline GR α LBD can be used to design compounds that bind to a GR LBD (more preferably a GR α LBD) and alter the properties of a GR LBD (for example, the dimerization ability, ligand binding ability or effect on transcription) in different ways. One aspect of the present invention provides for the design of compounds that can compete with natural or engineered ligands of a GR polypeptide by binding to all, or a portion of, the binding sites on a GR LBD. The present invention also provides for the design of compounds that can bind to all, or a portion of, an accessory binding site on a GR that is already binding a ligand. Similarly, non-competitive agonists/ligands that bind to and modulate GR LBD activity, whether or not it is bound to another chemical entity, and partial

agonists and antagonists can be designed using the GR LBD structure coordinates of this invention.

5 A second design approach is to probe an NR, SR or GR or an NR, SR or GR LBD (preferably a GR α or GR α LBD) crystal with molecules comprising a variety of different chemical entities to determine optimal sites for interaction between candidate NR, SR or GR or NR, SR or GR LBD modulators and the polypeptide. For example, high resolution X-ray diffraction data collected from crystals saturated with solvent allows the determination of the site where each type of solvent molecule adheres. Small molecules that bind tightly to those sites
10 can then be designed and synthesized and tested for their an NR, SR or GR modulator activity. Representative designs are also disclosed in published PCT application WO 99/26966.

Once a computationally-designed ligand is synthesized using the methods of the present invention or other methods known to those of skill in the art, assays
15 can be used to establish its efficacy of the ligand as a modulator of NR, SR or GR (preferably GR α) activity. After such assays, the ligands can be further refined by generating intact NR, SR or GR, or NR, SR or GR LBD, crystals with a ligand bound to the LBD. The structure of the ligand can then be further refined using the chemical modification methods described herein and known to those of skill in
20 the art, in order to improve the modulation activity or the binding affinity of the ligand. This process can lead to second generation ligands with improved properties.

Ligands also can be selected that modulate NR, SR or GR responsive gene transcription by the method of altering the interaction of co-activators and
25 co-repressors with their cognate NR, SR or GR. For example, agonistic ligands can be selected that block or dissociate a co-repressor from interacting with a GR, and/or that promote binding or association of a co-activator. Antagonistic ligands can be selected that block co-activator interaction and/or promote co-repressor interaction with a target receptor. Selection can be done via binding assays that
30 screen for designed ligands having the desired modulatory properties. Preferably, interactions of a GR α polypeptide are targeted. A suitable assay for screening that can be employed, *mutatis mutandis* in the present invention, as described in Oberfield, J.L., et al., *Proc Natl Acad Sci U S A.* (1999) May 25; 96(11):6102-6,

incorporated herein in its entirety by reference. Other examples of suitable screening assays for GR function include an *in vitro* peptide binding assay representing ligand-induced interaction with coactivator (Zhou, et al., (1998) *Mol. Endocrinol.* 12: 1594-1604; Parks et al., (1999) *Science* 284: 1365-1368) or a cell-based reporter assay related to transcription from a GRE (reviewed in Jenkins et al., (2001) *Trends Endocrinol. Metab.* 12: 122-126) or a cell-based reporter assay related to repression of genes driven via NF-kB. DeBosscher et al., (2000) *Proc Natl Acad Sci U S A.* 97: 3919-3924.

10 IX.A.3. Methods of Designing NR, SR or GR LBD Modulator
Compounds

Knowledge of the three-dimensional structure of the GR LBD complex of the present invention can facilitate a general model for modulator (e.g. agonist, partial agonist, antagonist and partial antagonist) design. Other ligand-receptor complexes belonging to the nuclear receptor superfamily can have a ligand binding pocket similar to that of GR and therefore the present invention can be employed in agonist/antagonist design for other members of the nuclear receptor superfamily and the steroid receptor subfamily. Examples of suitable receptors include those of the NR superfamily and those of the SR subfamily.

20 The design of candidate substances, also referred to as "compounds" or "candidate compounds", that bind to or inhibit NR, SR or GR LBD-mediated activity according to the present invention generally involves consideration of two factors. First, the compound must be capable of physically and structurally associating with a NR, SR or GR LBD. Non-covalent molecular interactions
25 important in the association of a NR, SR or GR LBD with its substrate include hydrogen bonding, van der Waals interactions and hydrophobic interactions.

The interaction between an atom of a LBD amino acid and an atom of an LBD ligand can be made by any force or attraction described in nature. Usually the interaction between the atom of the amino acid and the ligand will be the result of a hydrogen bonding interaction, charge interaction, hydrophobic interaction, van der Waals interaction or dipole interaction. In the case of the hydrophobic interaction it is recognized that this is not a per se interaction between the amino acid and ligand, but rather the usual result, in part, of the repulsion of water or

other hydrophilic group from a hydrophobic surface. Reducing or enhancing the interaction of the LBD and a ligand can be measured by calculating or testing binding energies, computationally or using thermodynamic or kinetic methods as known in the art.

5 Second, the compound must be able to assume a conformation that allows it to associate with a NR, SR or GR LBD. Although certain portions of the compound will not directly participate in this association with a NR, SR or GR LBD, those portions can still influence the overall conformation of the molecule. This, in turn, can have a significant impact on potency. Such conformational
10 requirements include the overall three-dimensional structure and orientation of the chemical entity or compound in relation to all or a portion of the binding site, e.g., the ligand binding pocket or an accessory binding site of a NR, SR or GR LBD, or the spacing between functional groups of a compound comprising several chemical entities that directly interact with a NR, SR or GR LBD.

15 Chemical modifications will often enhance or reduce interactions of an atom of a LBD amino acid and an atom of an LBD ligand. Steric hinderance can be a common means of changing the interaction of a LBD binding pocket with an activation domain. Chemical modifications are preferably introduced at C-H, C- and C-OH positions in a ligand, where the carbon is part of the ligand structure
20 that remains the same after modification is complete. In the case of C-H, C could have 1, 2 or 3 hydrogens, but usually only one hydrogen will be replaced. The H or OH can be removed after modification is complete and replaced with a desired chemical moiety.

 The potential modulatory or binding effect of a chemical compound on a
25 NR, SR or GR LBD can be analyzed prior to its actual synthesis and testing by the use of computer modeling techniques that employ the coordinates of a crystalline GR α LBD polypeptide of the present invention. If the theoretical structure of the given compound suggests insufficient interaction and association between it and a NR, SR or GR LBD, synthesis and testing of the compound is obviated. However,
30 if computer modeling indicates a strong interaction, the molecule can then be synthesized and tested for its ability to bind and modulate the activity of a NR, SR or GR LBD. In this manner, synthesis of unproductive or inoperative compounds can be avoided.

A modulatory or other binding compound of a NR, SR or GR LBD polypeptide (preferably a GR α LBD) can be computationally evaluated and designed via a series of steps in which chemical entities or fragments are screened and selected for their ability to associate with an individual binding site
5 or other area of a crystalline GR α LBD polypeptide of the present invention and to interact with the amino acids disposed in the binding sites.

Interacting amino acids forming contacts with a ligand and the atoms of the interacting amino acids are usually 2 to 4 angstroms away from the center of the atoms of the ligand. Generally these distances are determined by computer as
10 discussed herein and in McRee (McRee, (1993) *Practical Protein Crystallography*, Academic Press, New York), however distances can be determined manually once the three dimensional model is made. More commonly, the atoms of the ligand and the atoms of interacting amino acids are 3 to 4 angstroms apart. A ligand can also interact with distant amino acids, after chemical modification of the
15 ligand to create a new ligand. Distant amino acids are generally not in contact with the ligand before chemical modification. A chemical modification can change the structure of the ligand to make as new ligand that interacts with a distant amino acid usually at least 4.5 angstroms away from the ligand. Often distant amino acids will not line the surface of the binding cavity for the ligand, as they are too
20 far away from the ligand to be part of a pocket or surface of the binding cavity.

A variety of methods can be used to screen chemical entities or fragments for their ability to associate with an NR, SR or GR LBD and, more particularly, with the individual binding sites of an NR, SR or GR LBD, such as ligand binding pocket or an accessory binding site. This process can begin by visual inspection
25 of, for example, the ligand binding pocket on a computer screen based on the GR α LBD atomic coordinates in Table 4, as described herein. Selected fragments or chemical entities can then be positioned in a variety of orientations, or docked, within an individual binding site of a GR α LBD as defined herein above. Docking can be accomplished using software programs such as those
30 available under the tradenames QUANTA™ (Molecular Simulations Inc., San Diego, California) and SYBYL™ (Tripos, Inc., St. Louis, Missouri), followed by energy minimization and molecular dynamics with standard molecular mechanics forcefields, such as CHARM (Brooks et al., (1983) *J. Comp. Chem.*, 8: 132) and

AMBER 5 (Case et al., (1997), AMBER 5, University of California, San Francisco; Pearlman et al., (1995) *Comput. Phys. Commun.* 91: 1-41).

Specialized computer programs can also assist in the process of selecting fragments or chemical entities. These include:

- 5 1. GRID™ program, version 17 (Goodford, (1985) *J. Med. Chem.* 28: 849-57), which is available from Molecular Discovery Ltd., Oxford, UK;
2. MCSS™ program (Miranker & Karplus, (1991) *Proteins* 11: 29-34), which is available from Molecular Simulations, Inc., San Diego, California;
3. AUTODOCK™ 3.0 program (Goodsell & Olsen, (1990) *Proteins* 8: 195-10 202), which is available from the Scripps Research Institute, La Jolla, California;
4. DOCK™ 4.0 program (Kuntz et al., (1992) *J. Mol. Biol.* 161: 269-88), which is available from the University of California, San Francisco, California;
5. FLEX-X™ program (See, Rarey et al., (1996) *J. Comput. Aid. Mol. Des.* 10:41-54), which is available from Tripos, Inc., St. Louis, Missouri;
- 15 6. MVP program (Lambert, (1997) in Practical Application of Computer-Aided Drug Design, (Charifson, ed.) Marcel-Dekker, New York, pp. 243-303); and
7. LUDI™ program (Bohm, (1992) *J. Comput. Aid. Mol. Des.*, 6: 61-78), which is available from Molecular Simulations, Inc., San Diego, California.

20 Once suitable chemical entities or fragments have been selected, they can be assembled into a single compound or modulator. Assembly can proceed by visual inspection of the relationship of the fragments to each other on the three-dimensional image displayed on a computer screen in relation to the structure coordinates of a GR α LBD. Manual model building using software such as QUANTA™ or SYBYL™ typically follows.

25 Useful programs to aid one of ordinary skill in the art in connecting the individual chemical entities or fragments include:

1. CAVEAT™ program (Bartlett et al., (1989) *Special Pub.*, Royal Chem. Soc. 78: 182-96), which is available from the University of California, Berkeley, California;
- 30 2. 3D Database systems, such as MACCS-3D™ system program, which is available from MDL Information Systems, San Leandro, California. This area is reviewed in Martin, (1992) *J. Med. Chem.* 35: 2145-54; and

3. HOOK™ program (Eisen et al., (1994). *Proteins* 19: 199-221), which is available from Molecular Simulations, Inc., San Diego, California.

Instead of proceeding to build a GR LBD modulator (preferably a GR α LBD modulator) in a step-wise fashion one fragment or chemical entity at a time as described above, modulatory or other binding compounds can be designed as a whole or *de novo* using the structural coordinates of a crystalline GR α LBD polypeptide of the present invention and either an empty binding site or optionally including some portion(s) of a known modulator(s). Applicable methods can employ the following software programs:

1. LUDI™ program (Bohm, (1992) *J. Comput. Aid. Mol. Des.*, 6: 61-78), which is available from Molecular Simulations, Inc., San Diego, California;
2. LEGEND™ program (Nishibata & Itai, (1991) *Tetrahedron* 47: 8985); and
3. LEAPFROG™, which is available from Tripos Associates, St. Louis, Missouri.

Other molecular modeling techniques can also be employed in accordance with this invention. See, e.g., Cohen et al., (1990) *J. Med. Chem.* 33: 883-94. See also, Navia & Murcko, (1992) *Curr. Opin. Struc. Biol.* 2: 202-10; U.S. Patent No. 6,008,033, herein incorporated by reference.

- Once a compound has been designed or selected by the above methods, the efficiency with which that compound can bind to a NR, SR or GR LBD can be tested and optimized by computational evaluation. By way of particular example, a compound that has been designed or selected to function as a NR, SR or GR LBD modulator should also preferably traverse a volume not overlapping that occupied by the binding site when it is bound to its native ligand. Additionally, an effective NR, SR or GR LBD modulator should preferably demonstrate a relatively small difference in energy between its bound and free states (i.e., a small deformation energy of binding). Thus, the most efficient NR, SR and GR LBD modulators should preferably be designed with a deformation energy of binding of not greater than about 10 kcal/mole, and preferably, not greater than 7 kcal/mole. It is possible for NR, SR and GR LBD modulators to interact with the polypeptide in more than one conformation that is similar in overall binding energy. In those cases, the deformation energy of binding is taken to be the difference between the

energy of the free compound and the average energy of the conformations observed when the modulator binds to the polypeptide.

A compound designed or selected as binding to an NR, SR or GR polypeptide (preferably a GR α LBD polypeptide) can be further computationally
5 optimized so that in its bound state it would preferably lack repulsive electrostatic interaction with the target polypeptide. Such non-complementary (e.g., electrostatic) interactions include repulsive charge-charge, dipole-dipole and charge-dipole interactions. Specifically, the sum of all electrostatic interactions between the modulator and the polypeptide when the modulator is bound to an
10 NR, SR or GR LBD preferably make a neutral or favorable contribution to the enthalpy of binding.

Specific computer software is available in the art to evaluate compound deformation energy and electrostatic interaction. Examples of programs designed for such uses include:

- 15 1. Gaussian 98™, which is available from Gaussian, Inc., Pittsburgh, Pennsylvania;
2. AMBER™ program, version 6.0, which is available from the University of California at San Francisco;
3. QUANTA™ program, which is available from Molecular Simulations,
20 Inc., San Diego, California;
4. CHARMM® program, which is available from Molecular Simulations, Inc., San Diego, California; and
4. Insight II® program, which is available from Molecular Simulations, Inc., San Diego, California.

25 These programs can be implemented using a suitable computer system. Other hardware systems and software packages will be apparent to those skilled in the art after review of the disclosure of the present invention presented herein.

Once an NR, SR or GR LBD modulating compound has been optimally selected or designed, as described above, substitutions can then be made in
30 some of its atoms or side groups in order to improve or modify its binding properties. Generally, initial substitutions are conservative, i.e., the replacement group will have approximately the same size, shape, hydrophobicity and charge as the original group. It should, of course, be understood that components known

in the art to alter conformation are preferably avoided. Such substituted chemical compounds can then be analyzed for efficiency of fit to an NR, SR or GR LBD binding site using the same computer-based approaches described in detail above.

5

IX.B. Distinguishing Between GR Subtypes and Between NRs

The present invention also is applicable to generating new synthetic ligands to distinguish nuclear receptor subtypes. As described herein, modulators can be generated that distinguish between subtypes, thereby allowing the generation of
10 either tissue specific or function specific synthetic ligands. For instance, the GR α gene can be translated from its mRNA by alternative initiation from an internal ATG codon (Yudt & Cidlowski (2001) *Molec. Endocrinol.* 15: 1093-1103). This codon codes for methionine at position 27 and translation from this position produces a slightly smaller protein. These two isoforms, translated from the same
15 gene, are referred to as GR-A and GR-B. It has been shown in a cellular system that the shorter GR-B form is more effective in initiating transcription from a GRE compared to GR-A. Additionally, another form of GR, called GR β is produced by an alternative splicing event. The GR β protein differs from GR α at the very C-terminus, where the final 50 amino acids are replaced with a 15 amino acid
20 segment. These two isoforms are 100% identical up to amino acid 727. No sequence similarity exists between GR α and GR β at the C-terminus beyond position 727. GR β has been shown to be a dominant negative regulator of GR α -mediated gene transcription (Oakley, Sar & Cidlowski (1996) *J. Biol. Chem.* 271: 9550-9559). It has been suggested that some of the tissue specific effects
25 observed with glucocorticoid treatment may in part be due to the presence of varying amounts of isoform in certain cell-types. This method is also applicable to any other subfamily so organized.

The present invention discloses the ability to generate new synthetic ligands to distinguish between GR subtypes. As described herein, computer-
30 designed ligands (i.e. candidate modulators and modulators) can be generated that distinguish between GR subtypes, thereby allowing the generation of either tissue specific or function specific ligands. The atomic structural coordinates disclosed in the present invention reveal structural details unique to GR α . These

structural details can be exploited when a novel ligand is designed using the methods of the present invention or other ligand design methods known in the art. The structural features that differentiate, for example, a GR α from a GR β can be targeted in ligand design. Thus, for example, a ligand can be designed that will
5 recognize GR α , while not interacting with other GRs or even with moieties having similar structural features. Prior to the disclosure of the present invention, the ability to target a GR subtype was unattainable.

The present invention also pertains to a method for designing an agonist or modulator with desired levels of activity on at least two subtypes, GR α and GR β .
10 In a preferred embodiment, the method comprises obtaining atomic coordinates for structures of the GR α and/or GR β ligand binding domains. The structures can comprise GR α and GR β , each bound to various different ligands, and also can comprise structures where no ligand is present. The structures can also comprise models where a compound has been docked into a particular GR using a
15 molecular docking procedure, such as the MVP program disclosed herein. Optionally, the structures are rotated and translated so as to superimpose corresponding C α or backbone atoms; this facilitates the comparison of structures.

The GR α and GR β structures can also be compared using a computer
20 graphics system to identify regions of the ligand binding site that have similar shape and electrostatic character, and to identify regions of the ligand binding site that are narrowed or constricted in one or both of the GRs, particularly as compared to other NRs. Since these three GRs are subject to conformational changes, attention is paid to the range of motion observed for each protein atom
25 over the whole collection of structures. The ligand structures, including both those determined by X-ray crystallography and those modeled using molecular docking procedures, can be examined using a computer graphics system to identify ligands where a chemical modification could increase or decrease binding to a particular GR, or decrease activity against a particular GR. Additionally or
30 alternatively, the chemical modification can introduce a group into a volume that is normally occupied by an atom of that GR.

Optionally, to selectively decrease activity against a particular GR, the chemical modification can be made so as to occupy volume that is normally

occupied by atoms of that particular GR, but not by atoms of the other GRs. To increase activity against a particular GR, a chemical modification can be made that improves interactions with that particular GR. To selectively increase activity against a particular GR, a chemical modification can be made that improves the interactions with that particular GR, but does not improve the interactions with the other GRs. Other design principles can also be used to increase or decrease activity on a particular GR.

Thus, various possible compounds and chemical modifications can be considered and compared graphically, and with molecular modeling tools, for synthetic feasibility and likelihood of achieving the desired profile of activation of GR α and GR β . Compounds that appear synthetically feasible and that have a good likelihood of achieving the desired profile are synthesized. The compounds can then be tested for binding and/or activation of GR α and GR β , and tested for their overall biological effect.

A method of identifying a NR modulator that selectively modulates the biological activity of one NR compared to GR α is also disclosed. In one embodiment, the method comprises: (a) providing an atomic structure coordinate set describing a GR α ligand binding domain structure and at least one other atomic structure coordinate set describing a NR ligand binding domain, each ligand binding domain comprising a ligand binding site; (b) comparing the atomic structure coordinate sets to identify at least one difference between the sets; (c) designing a candidate ligand predicted to interact with the difference of step (b); (d) synthesizing the candidate ligand; and (e) testing the synthesized candidate ligand for an ability to selectively modulate a NR as compared to GR α , whereby a NR modulator that selectively modulates the biological activity NR compared to GR α is identified.

Preferably, the GR α atomic structure coordinate set is the atomic structure coordinate set shown in Table 4. Optionally, the NR is selected from the group consisting of MR, PR, AR, GR β and isoforms thereof that have ligands that also bind GR α .

IX.C. Method of Screening for Chemical and Biological Modulators of the Biological Activity of an NR, SR or GR

A candidate substance identified according to a screening assay of the present invention has an ability to modulate the biological activity of an NR, SR or GR or an NR, SR or GR LBD polypeptide. In a preferred embodiment, such a candidate compound can have utility in the treatment of disorders and/or conditions and/or biological events associated with the biological activity of an NR, SR or GR or an NR, SR or GR LBD polypeptide, including transcription modulation.

10 In a cell-free system, the method comprises the steps of establishing a control system comprising a GR α polypeptide and a ligand which is capable of binding to the polypeptide; establishing a test system comprising a GR α polypeptide, the ligand, and a candidate compound; and determining whether the candidate compound modulates the activity of the polypeptide by comparison of
15 the test and control systems. A representative ligand can comprise dexamethasone or other small molecule, and in this embodiment, the biological activity or property screened can include binding affinity or transcription regulation. The GR α polypeptide can be in soluble or crystalline form.

In another embodiment of the invention, a soluble or a crystalline form of a GR α polypeptide or a catalytic or immunogenic fragment or oligopeptide thereof,
20 can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such a screening can be affixed to a solid support. The formation of binding complexes, between a soluble or a crystalline GR α polypeptide and the agent being tested, will be detected. In a
25 preferred embodiment, the soluble or crystalline GR α polypeptide has an amino acid sequence of any of SEQ ID NOs:4, 6, 8 or 10. When a GR α LBD polypeptide is employed, a preferred embodiment will include a soluble or a crystalline GR α polypeptide having the amino acid sequence of any of SEQ ID NOs:12, 14, 16 or 31.

30 Another technique for drug screening which can be used provides for high throughput screening of compounds having suitable binding affinity to the protein of interest as described in published PCT application WO 84/03564, herein incorporated by reference. In this method, as applied to a soluble or crystalline

polypeptide of the present invention, large numbers of different small test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The test compounds are reacted with the soluble or crystalline polypeptide, or fragments thereof. Bound polypeptide is then detected by
5 methods known to those of skill in the art. The soluble or crystalline polypeptide can also be placed directly onto plates for use in the aforementioned drug screening techniques.

In yet another embodiment, a method of screening for a modulator of an NR, SR or GR or an NR, SR or GR LBD polypeptide comprises: providing a library
10 of test samples; contacting a soluble or a crystalline form of an NR, SR or GR or a soluble or crystalline form of an NR, SR or GR LBD polypeptide with each test sample; detecting an interaction between a test sample and a soluble or a crystalline form of an NR, SR or GR or a soluble or a crystalline form of an NR, SR or GR LBD polypeptide; identifying a test sample that interacts with a soluble
15 or a crystalline form of an NR, SR or GR or a soluble or a crystalline form of an NR, SR or GR LBD polypeptide; and isolating a test sample that interacts with a soluble or a crystalline form of an NR, SR or GR or a soluble or a crystalline form of an NR, SR or GR LBD polypeptide.

In each of the foregoing embodiments, an interaction can be detected
20 spectrophotometrically, radiologically, colorimetrically or immunologically. An interaction between a soluble or a crystalline form of an NR, SR or GR or a soluble or a crystalline form of an NR, SR or GR LBD polypeptide and a test sample can also be quantified using methodology known to those of skill in the art.

In accordance with the present invention there is also provided a rapid and
25 high throughput screening method that relies on the methods described above. This screening method comprises separately contacting each of a plurality of substantially identical samples with a soluble or a crystalline form of an NR, SR or GR or a soluble or a crystalline form of an NR, SR or GR LBD and detecting a resulting binding complex. In such a screening method the plurality of samples
30 preferably comprises more than about 10^4 samples, or more preferably comprises more than about 5×10^4 samples.

In another embodiment, a method for identifying a substance that modulates GR LBD function is also provided. In a preferred embodiment, the

- method comprises: (a) isolating a GR polypeptide of the present invention; (b) exposing the isolated GR polypeptide to a plurality of substances; (c) assaying binding of a substance to the isolated GR polypeptide; and (d) selecting a substance that demonstrates specific binding to the isolated GR LBD polypeptide.
- 5 By the term "exposing the GR polypeptide to a plurality of substances", it is meant both in pools and as multiple samples of "discrete" pure substances.

IX.D. Method of Identifying Compounds Which Inhibit Ligand Binding

- In one aspect of the present invention, an assay method for identifying a
- 10 compound that inhibits binding of a ligand to an NR, SR or GR polypeptide is disclosed. A ligand, such as dexamethasone (which associates with at least GR), can be used in the assay method as the ligand against which the inhibition by a test compound is gauged. In the following discussion of Section IX.D., it will be understood that although GR is used as an example, the method is equally
- 15 applicable to any of NR, SR or GR polypeptide. The method comprises (a) incubating a GR polypeptide with a ligand in the presence of a test inhibitor compound; (b) determining an amount of ligand that is bound to the GR polypeptide, wherein decreased binding of ligand to the GR polypeptide in the presence of the test inhibitor compound relative to binding in the absence of the
- 20 test inhibitor compound is indicative of inhibition; and (c) identifying the test compound as an inhibitor of ligand binding if decreased ligand binding is observed. Preferably, the ligand is dexamethasone.

- In another aspect of the present invention, the disclosed assay method can be used in the structural refinement of candidate GR inhibitors. For example,
- 25 multiple rounds of optimization can be followed by gradual structural changes in a strategy of inhibitor design. A strategy such as this is made possible by the disclosure of the atomic coordinates of the GR α LBD.

X. Design, Preparation and Structural Analysis of Additional NR, SR and GR Polypeptides and NR, SR and GR LBD Mutants and Structural Equivalents

- 30 The present invention provides for the generation of NR, SR and GR polypeptides and NR, SR or GR mutants (preferably GR α and GR α LBD

mutants), and the ability to solve the crystal structures of those that crystallize. Indeed, a GR α LBD having a point mutation was crystallized and solved in one aspect of the present invention. Thus, an aspect of the present invention involves the use of both targeted and random mutagenesis of the GR gene for the production of a recombinant protein with improved or desired characteristics for the purpose of crystallization, characterization of biologically relevant protein-protein interactions, and compound screening assays, or for the production of a recombinant protein having other desirable characteristic(s). Polypeptide products produced by the methods of the present invention are also disclosed herein.

The structure coordinates of a NR, SR or GR LBD provided in accordance with the present invention also facilitate the identification of related proteins or enzymes analogous to GR α in function, structure or both, (for example, a GR β) which can lead to novel therapeutic modes for treating or preventing a range of disease states. More particularly, through the provision of the mutagenesis approaches as well as the three-dimensional structure of a GR α LBD disclosed herein, desirable sites for mutation are identified.

X.A. Sterically Similar Compounds

A further aspect of the present invention is that sterically similar compounds can be formulated to mimic the key portions of an NR, SR or GR LBD structure. Such compounds are functional equivalents. The generation of a structural functional equivalent can be achieved by the techniques of modeling and chemical design known to those of skill in the art and described herein. Modeling and chemical design of NR, SR or GR and NR, SR or GR LBD structural equivalents can be based on the structure coordinates of a crystalline GR α LBD polypeptide of the present invention. It will be understood that all such sterically similar constructs fall within the scope of the present invention.

X.B. NR, SR and GR Polypeptides

The generation of chimeric GR polypeptides is also an aspect of the present invention. Such a chimeric polypeptide can comprise an NR, SR or GR LBD polypeptide or a portion of an NR, SR or GR LBD, (e.g. a GR α LBD) that is

fused to a candidate polypeptide or a suitable region of the candidate polypeptide, for example GR β . Throughout the present disclosure it is intended that the term "mutant" encompass not only mutants of an NR, SR or GR LBD polypeptide but chimeric proteins generated using an NR, SR or GR LBD as well. It is thus
5 intended that the following discussion of mutant NR, SR and GR LBDs apply *mutatis mutandis* to chimeric NR, SR and GR polypeptides and NR, SR and GR LBD polypeptides and to structural equivalents thereof.

In accordance with the present invention, a mutation can be directed to a particular site or combination of sites of a wild-type NR, SR or GR LBD. For
10 example, an accessory binding site or the binding pocket can be chosen for mutagenesis. Similarly, a residue having a location on, at or near the surface of the polypeptide can be replaced, resulting in an altered surface charge of one or more charge units, as compared to the wild-type NR, SR or GR and NR, SR or GR LBDs. Alternatively, an amino acid residue in an NR, SR or GR or an NR, SR
15 or GR LBD can be chosen for replacement based on its hydrophilic or hydrophobic characteristics.

Such mutants can be characterized by any one of several different properties, i.e. a "desired" or "predetermined" characteristic as compared with the wild type NR, SR or GR LBD. For example, such mutants can have an altered
20 surface charge of one or more charge units, or can have an increase in overall stability. Other mutants can have altered substrate specificity in comparison with, or a higher specific activity than, a wild-type NR, SR or GR or an NR, SR or GR LBD.

NR, SR or GR and NR, SR or GR LBD mutants of the present invention
25 can be generated in a number of ways. For example, the wild-type sequence of an NR, SR or GR or an NR, SR or GR LBD can be mutated at those sites identified using this invention as desirable for mutation, by means of oligonucleotide-directed mutagenesis or other conventional methods, such as deletion. Alternatively, mutants of an NR, SR or GR or an NR, SR or GR LBD can
30 be generated by the site-specific replacement of a particular amino acid with an unnaturally occurring amino acid. In addition, NR, SR or GR or NR, SR or GR LBD mutants can be generated through replacement of an amino acid residue, for example, a particular cysteine or methionine residue, with selenocysteine or

selenomethionine. This can be achieved by growing a host organism capable of expressing either the wild-type or mutant polypeptide on a growth medium depleted of either natural cysteine or methionine (or both) but enriched in selenocysteine or selenomethionine (or both).

5 As disclosed in the Examples presented below, mutations can be introduced into a DNA sequence coding for an NR, SR or GR or an NR, SR or GR LBD using synthetic oligonucleotides. These oligonucleotides contain nucleotide sequences flanking the desired mutation sites. Mutations can be generated in the full-length DNA sequence of an NR, SR or GR or an NR, SR or GR LBD or in any
10 sequence coding for polypeptide fragments of an NR, SR or GR or an NR, SR or GR LBD.

 According to the present invention, a mutated NR, SR or GR or NR, SR or GR LBD DNA sequence produced by the methods described above, or any alternative methods known in the art, can be expressed using an expression
15 vector. An expression vector, as is well known to those of skill in the art, typically includes elements that permit autonomous replication in a host cell independent of the host genome, and one or more phenotypic markers for selection purposes. Either prior to or after insertion of the DNA sequences surrounding the desired NR, SR or GR or NR, SR or GR LBD mutant coding sequence, an expression
20 vector also will include control sequences encoding a promoter, operator, ribosome binding site, translation initiation signal, and, optionally, a repressor gene or various activator genes and a signal for termination. In some embodiments, where secretion of the produced mutant is desired, nucleotides encoding a "signal sequence" can be inserted prior to an NR, SR or GR or an NR,
25 SR or GR LBD mutant coding sequence. For expression under the direction of the control sequences, a desired DNA sequence must be operatively linked to the control sequences; that is, the sequence must have an appropriate start signal in front of the DNA sequence encoding the NR, SR or GR or NR, SR or GR LBD mutant, and the correct reading frame to permit expression of that sequence
30 under the control of the control sequences and production of the desired product encoded by that NR, SR or GR or NR, SR or GR LBD sequence must be maintained.

After a review of the disclosure of the present invention presented herein, any of a wide variety of well-known available expression vectors can be useful to express a mutated coding sequence of this invention. These include for example, vectors consisting of segments of chromosomal, non-chromosomal and synthetic
5 DNA sequences, such as various known derivatives of SV40, known bacterial plasmids, e.g., plasmids from *E. coli* including col E1, pCR1, pBR322, pMB9 and their derivatives, wider host range plasmids, e.g., RP4, phage DNAs, e.g., the numerous derivatives of phage λ , e.g., NM 989, and other DNA phages, e.g., M13 and filamentous single stranded DNA phages, yeast plasmids and vectors derived
10 from combinations of plasmids and phage DNAs, such as plasmids which have been modified to employ phage DNA or other expression control sequences. In the preferred embodiments of this invention, vectors amenable to expression in a pET-based expression system are employed. The pET expression system is available from Novagen/Invitrogen, Inc., Carlsbad, California. Expression and
15 screening of a polypeptide of the present invention in bacteria, preferably *E. coli*, is a preferred aspect of the present invention.

In addition, any of a wide variety of expression control sequences—sequences that control the expression of a DNA sequence when operatively linked to it—can be used in these vectors to express the mutated DNA sequences
20 according to this invention. Such useful expression control sequences, include, for example, the early and late promoters of SV40 for animal cells, the lac system, the trp system the TAC or TRC system, the major operator and promoter regions of phage λ , the control regions of fd coat protein, all for *E. coli*, the promoter for 3-phosphoglycerate kinase or other glycolytic enzymes, the promoters of acid
25 phosphatase, e.g., Pho5, the promoters of the yeast α -mating factors for yeast, and other sequences known to control the expression of genes of prokaryotic or eukaryotic cells or their viruses, and various combinations thereof.

A wide variety of hosts are also useful for producing mutated NR, SR or GR and NR, SR or GR LBD polypeptides according to this invention. These hosts
30 include, for example, bacteria, such as *E. coli*, *Bacillus* and *Streptomyces*, fungi, such as yeasts, and animal cells, such as CHO and COS-1 cells, plant cells, insect cells, such as SF9 cells, and transgenic host cells. Expression and

screening of a polypeptide of the present invention in bacteria, preferably *E. coli*, is a preferred aspect of the present invention.

It should be understood that not all expression vectors and expression systems function in the same way to express mutated DNA sequences of this invention, and to produce modified NR, SR or GR and NR, SR or GR LBD polypeptides or NR, SR or GR or NR, SR or GR LBD mutants. Neither do all hosts function equally well with the same expression system. One of skill in the art can, however, make a selection among these vectors, expression control sequences and hosts without undue experimentation and without departing from the scope of this invention. For example, an important consideration in selecting a vector will be the ability of the vector to replicate in a given host. The copy number of the vector, the ability to control that copy number, and the expression of any other proteins encoded by the vector, such as antibiotic markers, should also be considered.

In selecting an expression control sequence, a variety of factors should also be considered. These include, for example, the relative strength of the system, its controllability and its compatibility with the DNA sequence encoding a modified NR, SR or GR or NR, SR or GR LBD polypeptide of this invention, with particular regard to the formation of potential secondary and tertiary structures.

Hosts should be selected by consideration of their compatibility with the chosen vector, the toxicity of a modified polypeptide to them, their ability to express mature products, their ability to fold proteins correctly, their fermentation requirements, the ease of purification of a modified GR or GR LBD and safety. Within these parameters, one of skill in the art can select various vector/expression control system/host combinations that will produce useful amounts of a mutant polypeptide. A mutant polypeptide produced in these systems can be purified, for example, via the approaches disclosed in the Examples.

Once a mutation(s) has been generated in the desired location, such as an active site or dimerization site, the mutants can be tested for any one of several properties of interest, i.e. "desired" or "predetermined" positions. For example, mutants can be screened for an altered charge at physiological pH. This property can be determined by measuring the mutant polypeptide isoelectric point (pI) and

comparing the observed value with that of the wild-type parent. Isoelectric point can be measured by gel-electrophoresis according to the method of Wellner (Wellner, (1971) *Anal. Chem.* 43: 597). A mutant polypeptide containing a replacement amino acid located at the surface of the enzyme, as provided by the structural information of this invention, can lead to an altered surface charge and an altered pl.

X.C. Generation of an Engineered NR, SR or GR or NR, SR or GR LBD Mutants

10 In another aspect of the present invention, a unique NR, SR or GR or NR, SR or GR LBD polypeptide is generated. Such a mutant can facilitate purification and the study of the structure and the ligand-binding abilities of a NR, SR or GR polypeptide. Thus, an aspect of the present invention involves the use of both targeted and random mutagenesis of the GR gene for the production of a
15 recombinant protein with improved solution characteristics for the purpose of crystallization, characterization of biologically relevant protein-protein interactions, and compound screening assays , or for the production of a recombinant polypeptide having other characteristics of interest. Expression of the polypeptide in bacteria, preferably *E. coli*, is also an aspect of the present invention.

20 In one embodiment, targeted mutagenesis was performed using a sequence alignment of several nuclear receptors, primarily steroid receptors. Several residues that were hydrophobic in GR and hydrophilic in other receptors were chosen for mutagenesis. Most of these residues were predicted to be solvent exposed hydrophobic residues in GR. Therefore, mutations were made to
25 change these hydrophobic residues to hydrophilic in attempt to improve the solubility and stability of *E.coli*-expressed GR LBD. Table 2 immediately below presents a list of mutations (for that were made and tested for expression in *E. coli*).

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Table 2
Mutations of the GR LBD (521-777) Gene for
Testing Solution Solubility and Stability

Single mutations	Double mutations	Triple mutations
V552K	L535T/V538S	M691T/V702T/W712T
W557S	V552K/W557S	
F602S	L636E/C638S	
F602D		
F602E		
L636E		
Y648Q		
W712S		
L741R		
F602Y		
F602T		
F602N		
F602C		

Random mutagenesis can be performed on residues where a significant difference, hydrophobic versus hydrophilic, is observed between GR and other steroid receptors based on sequence alignment. Such positions can be randomized by oligo-directed or cassette mutagenesis. A GR LBD protein library
 5 can be sorted by an appropriate display system to select mutants with improved solution properties. Residues in GR that meet the criteria for such an approach include: V538, V552, W557, F602, L636, Y648, Y660, L685, M691, V702, W712, L733, and Y764. In addition, residues predicted to neighbor these positions could also be randomized.

10 In another embodiment, complete random mutagenesis can be performed on any residue within the context of the GR LBD. A method such as error incorporating PCR or chemical-based mutagenesis can be used to introduce mutations in an unbiased manner. These methods randomize the position of mutation as well as the nature of the mutated residue. A completely random GR
 15 LBD library can be screened for improved expression with the appropriate expression or display system. Ideally, the selection method should identify mutant proteins with increased expression, solubility, stability, and/or activity. A technique well suited for this purpose is the "peptides-on-plasmid" display system that utilizes the DNA-binding activity of the lac repressor (LacI). GR, or another
 20 nuclear receptor LBD, can be expressed as a fusion to either LacI or a fragment of LacI, such as the "headpiece dimer", that comprises the DNA-binding domain. Because the plasmid that expresses the fusion protein also comprises a lac operon binding site, the protein will be physically coupled to the plasmid. GR mutants that produce soluble protein can then be isolated using either the
 25 coactivator peptide- or ligand-binding activity of the receptor. Table 2A below shows mutations that were prepared using the LacI-based "peptides-on-plasmids" technique with GR LBD.

Table 2A

Random Mutations of the GR LBD (521-777) Gene for Improving

Solution Solubility and Stability

Single mutations	SEQ ID NO	Double Mutations	SEQ ID NO
W557R	33	F602L/A580T	38

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Q615L	34	L563F/G583C	39
Q615H	35	L664H/M752T	40
A574T	36	L563F/T744N	41
L620M	37		

5

A method of modifying a test NR polypeptide is thus disclosed. The method can comprise: providing a test NR polypeptide sequence having a characteristic that is targeted for modification; aligning the test NR polypeptide sequence with at least one reference NR polypeptide sequence for which an X-ray structure is available, wherein the at least one reference NR polypeptide sequence has a characteristic that is desired for the test NR polypeptide; building a three-dimensional model for the test NR polypeptide using the three-dimensional coordinates of the X-ray structure(s) of the at least one reference polypeptide and its sequence alignment with the test NR polypeptide sequence; examining the three-dimensional model of the test NR polypeptide for differences with the at least one reference polypeptide that are associated with the desired characteristic; and mutating at least one amino acid residue in the test NR polypeptide sequence located at a difference identified above to a residue associated with the desired characteristic, whereby the test NR polypeptide is modified. By the term "associated with a desired characteristic" it is meant that a residue is found in the reference polypeptide at a point of difference wherein the difference provides a desired characteristic or phenotype in the reference polypeptide.

A method of altering the solubility of a test NR polypeptide is also disclosed in accordance with the present invention. In a preferred embodiment, the method comprises: (a) providing a reference NR polypeptide sequence and a test NR polypeptide sequence; (b) comparing the reference NR polypeptide sequence and the test NR polypeptide sequence to identify one or more residues in the test NR sequence that are more or less hydrophilic than a corresponding residue in the reference NR polypeptide sequence; and (c) mutating the residue in the test NR polypeptide sequence identified in step (b) to a residue having a different hydrophilicity, whereby the solubility of the test NR polypeptide is altered.

By the term "altering" it is meant any change in the solubility of the test NR polypeptide, including preferably a change to make the polypeptide more soluble. Such approaches to obtain soluble proteins for crystallization studies have been successfully demonstrated in the case of HIV integration intergrase and the human leptin cytokine. See Dyda, F., et al., *Science* (1994) Dec 23; 266(5193):1981-6; and Zhang et al., *Nature* (1997) May 8; 387(6629):206-9.

Typically, such a change involves substituting a residue that is more hydrophilic than the wild type residue. Hydrophobicity and hydrophilicity criteria and comparison information are set forth herein below. Optionally, the reference NR polypeptide sequence is an AR or a PR sequence, and the test polypeptide sequence is a GR polypeptide sequence. Alternatively, the reference polypeptide sequence is a crystalline GR LBD. The comparing of step (b) is preferably by sequence alignment. More preferably, the screening is carried out in bacteria, even more preferably, in *E. coli*.

A method for modifying a test NR polypeptide to alter and preferably improve the solubility, stability in solution and other solution behavior, to alter and preferably improve the folding and stability of the folded structure, and to alter and preferably improve the ability to form ordered crystals is also provided in accordance with the present invention. The aforementioned characteristics are representative "desired" or "predetermined characteristics or phenotypes."

In a preferred embodiment, the method comprises:

- (a) providing a test NR polypeptide sequence for which the solubility, stability in solution, other solution behavior, tendency to fold properly, ability to form ordered crystals, or combination thereof is different from that desired;
- (b) aligning the test NR polypeptide sequence with the sequences of other reference NR polypeptides for which the X-ray structure is available and for which the solution properties, folding behavior and crystallization properties are closer to those desired;
- (c) building a three-dimensional model for the test NR polypeptide using the three-dimensional coordinates of the X-ray structure(s) of one or more of the reference polypeptides and their sequence alignment with the test NR polypeptide sequence;
- (d) optionally, optimizing the side-chain conformations in the three-

dimensional model by generating many alternative side-chain conformations, refining by energy minimization, and selecting side-chain conformations with lower energy;

5 (e) examining the three-dimensional model for the test NR graphically for lipophilic side-chains that are exposed to solvent, for clusters of two or more lipophilic side-chains exposed to solvent, for lipophilic pockets and clefts on the surface of the protein model, and in particular for sites on the surface of the protein model that are more lipophilic than the corresponding sites on the structure(s) of the reference NR polypeptide(s);

10 (f) for each residue identified in step (e), mutating the amino acid to an amino acid with different hydrophilicity, and usually to a more hydrophilic amino acid, whereby the exposed lipophilic sites are reduced, and the solution properties improved;

15 (g) examining the three-dimensional model graphically at each site where the amino acid in the test NR polypeptide is different from the amino acid at the corresponding position in the reference NR polypeptide, and checking whether the amino acid in the test NR polypeptide makes favorable interactions with the atoms that lie around it in the three-dimensional model, considering the side-chain conformations predicted in steps (c) and, optionally step (d), as well as likely
20 alternative conformations of the side-chains, and also considering the possible presence of water molecules (for this analysis, an amino acid is considered to make "favorable interactions with the atoms that lie around it" if these interactions are more favorable than the interactions that would be obtained if it was replaced by any of the 19 other naturally-occurring amino acids);

25 (h) for each residue identified in step (g) as not making favorable interactions with the atoms that lie around it, mutating the residue to another amino acid that could make better interactions with the atoms that lie around it, thereby promoting the tendency for the test NR polypeptide to fold into a stable structure with improved solution properties, less tendency to unfold, and greater
30 tendency to form ordered crystals;

(i) examining the three-dimensional model graphically at each residue position where the amino acid in the test NR polypeptide is different from the amino acid at the corresponding position in the reference NR polypeptide, and

checking whether the steric packing, hydrogen bonding and other energetic interactions could be improved by mutating that residue or any one or more of the surrounding residues lying within 8 angstroms in the three-dimensional model;

- (j) for each residue position identified in step (i) as potentially allowing an improvement in the packing, hydrogen bonding and energetic interactions, mutating those residues individually or in combination to residues that could improve the packing, hydrogen bonding and energetic interactions, thereby promoting the tendency for the test NR polypeptide to fold into a stable structure with improved solution properties, less tendency to unfold, and greater tendency to form ordered crystals.

By the term "graphically" it is meant through the use of computer aided graphics, such by the use of a software package disclosed herein above. Optionally, in this embodiment, the reference NR polypeptide is AR, or preferably PR, when the test NR polypeptide is GR α . Alternatively, the reference NR polypeptide is GR α , and the test NR polypeptide is GR β or MR.

An isolated GR polypeptide comprising a mutation in a ligand binding domain, wherein the mutation alters the solubility of the ligand binding domain, is also disclosed. An isolated GR polypeptide, or functional portion thereof, having one or more mutations comprising a substitution of a hydrophobic amino acid residue by a hydrophilic amino acid residue in a ligand binding domain is also disclosed. Preferably, in each case, the mutation can be at a residue selected from the group consisting of V552, W557, F602, L636, Y648, W712, L741, L535, V538, C638, M691, V702, Y648, Y660, L685, M691, V702, W712, L733, Y764 and combinations thereof. More preferably, the mutation is selected from the group consisting of V552K, W557S, F602S, F602D, F602E, F602Y, F602T, F602N, F602C, L636E, Y648Q, W712S, L741R, L535T, V538S, C638S, M691T, V702T, W712T and combinations thereof. Even more preferably, the mutation is made by targeted point or randomizing mutagenesis. Hydrophobicity and hydrophilicity criteria and comparison information are set forth herein below.

As discussed above, the GR α gene can be translated from its mRNA by alternative initiation from an internal ATG codon (Yudt & Cidlowski (2001) *Molec. Endocrinol.* 15: 1093-1103). This codon codes for methionine at position 27 and translation from this position produces a slightly smaller protein. These two

isoforms, translated from the same gene, are referred to as GR-A and GR-B. It has been shown in a cellular system that the shorter GR-B form is more effective in initiating transcription from a GRE compared to GR-A. Additionally, another form of GR, called GR β is produced by an alternative splicing event. The GR β protein differs from GR α at the very C-terminus, where the final 50 amino acids are replaced with a 15 amino acid segment. These two isoforms are 100% identical up to amino acid 727. No sequence similarity exists between GR α and GR β at the C-terminus beyond position 727. GR β has been shown to be a dominant negative regulator of GR α -mediated gene transcription (Oakley, Sar & Cidlowski (1996) *J. Biol. Chem.* 271: 9550-9559). It has been suggested that some of the tissue specific effects observed with glucocorticoid treatment may in part be due to the presence of varying amounts of isoform in certain cell-types. This method is also applicable to any other subfamily so organized. Thus, while the amino acid residue numbers referenced above pertain to GR-A, the polypeptides of the present invention also have a mutation at an analogous position in any polypeptide based on a sequence alignment (such as prepared by BLAST or other approach disclosed herein or known in the art) to GR α , which are not forth herein for convenience.

As used in the following discussion, the terms "engineered NR, SR or GR", "engineered NR, SR or GR LBD", "NR, SR or GR mutant", and "NR, SR or GR LBD mutant" refers to polypeptides having amino acid sequences that contain at least one mutation in the wild-type sequence, including at an analogous position in any polypeptide based on a sequence alignment to GR α . The terms also refer to NR, SR or GR and NR, SR or GR LBD polypeptides which are capable of exerting a biological effect in that they comprise all or a part of the amino acid sequence of an engineered mutant polypeptide of the present invention, or cross-react with antibodies raised against an engineered mutant polypeptide, or retain all or some or an enhanced degree of the biological activity of the engineered mutant amino acid sequence or protein. Such biological activity can include the binding of small molecules in general, the binding of glucocorticoids in particular and even more particularly the binding of dexamethasone.

The terms "engineered NR, SR or GR LBD" and "NR, SR or GR LBD mutant" also includes analogs of an engineered NR, SR or GR polypeptide or NR,

SR or GR LBD or GR LBD mutant polypeptide. By "analog" is intended that a DNA or polypeptide sequence can contain alterations relative to the sequences disclosed herein, yet retain all or some or an enhanced degree of the biological activity of those sequences. Analogs can be derived from genomic nucleotide sequences or from other organisms, or can be created synthetically. Those of skill in the art will appreciate that other analogs, as yet undisclosed or undiscovered, can be used to design and/or construct mutant analogs. There is no need for an engineered mutant polypeptide to comprise all or substantially all of the amino acid sequence of the wild type polypeptide (e.g. SEQ ID NOs:2 or 10). Shorter or longer sequences are anticipated to be of use in the invention; shorter sequences are herein referred to as "segments". Thus, the terms "engineered NR, SR or GR LBD" and "NR, SR or GR LBD mutant" also includes fusion, chimeric or recombinant engineered NR, SR or GR LBD or NR, SR or GR LBD mutant polypeptides and proteins comprising sequences of the present invention. Methods of preparing such proteins are disclosed herein above.

X.D. Sequence Similarity and Identity

As used herein, the term "substantially similar" as applied to GR means that a particular sequence varies from nucleic acid sequence of any of odd numbered SEQ ID NOs:1-15, or the amino acid sequence of any of even numbered SEQ ID NOs:2-16 by one or more deletions, substitutions, or additions, the net effect of which is to retain at least some of biological activity of the natural gene, gene product, or sequence. Such sequences include "mutant" or "polymorphic" sequences, or sequences in which the biological activity and/or the physical properties are altered to some degree but retains at least some or an enhanced degree of the original biological activity and/or physical properties. In determining nucleic acid sequences, all subject nucleic acid sequences capable of encoding substantially similar amino acid sequences are considered to be substantially similar to a reference nucleic acid sequence, regardless of differences in codon sequences or substitution of equivalent amino acids to create biologically functional equivalents.

X.D.1. Sequences That are Substantially Identical to an Engineered NR, SR or GR or NR, SR or GR LBD Mutant Sequence of the Present Invention

Nucleic acids that are substantially identical to a nucleic acid sequence of
5 an engineered NR, SR or GR or NR, SR or GR LBD mutant of the present
invention, e.g. allelic variants, genetically altered versions of the gene, etc., bind to
an engineered NR, SR or GR or NR, SR or GR LBD mutant sequence under
stringent hybridization conditions. By using probes, particularly labeled probes of
DNA sequences, one can isolate homologous or related genes. The source of
10 homologous genes can be any species, e.g. primate species; rodents, such as
rats and mice, canines, felines, bovines, equines, yeast, nematodes, etc.

Between mammalian species, e.g. human and mouse, homologs have
substantial sequence similarity, i.e. at least 75% sequence identity between
nucleotide sequences. Sequence similarity is calculated based on a reference
15 sequence, which can be a subset of a larger sequence, such as a conserved
motif, coding region, flanking region, etc. A reference sequence will usually be at
least about 18 nt long, more usually at least about 30 nt long, and can extend to
the complete sequence that is being compared. Algorithms for sequence analysis
are known in the art, such as BLAST, described in Altschul et al., (1990) *J. Mol.*
20 *Biol.* 215: 403-10. Software for performing BLAST analyses is publicly available
through the National Center for Biotechnology Information
(<http://www.ncbi.nlm.nih.gov/>).

This algorithm involves first identifying high scoring sequence pairs (HSPs)
by identifying short words of length W in the query sequence, which either match
25 or satisfy some positive-valued threshold score T when aligned with a word of the
same length in a database sequence. T is referred to as the neighborhood word
score threshold. These initial neighborhood word hits act as seeds for initiating
searches to find longer HSPs containing them. The word hits are then extended in
both directions along each sequence for as far as the cumulative alignment score
30 can be increased. Cumulative scores are calculated using, for nucleotide
sequences, the parameters M (reward score for a pair of matching residues;
always > 0) and N (penalty score for mismatching residues; always < 0). For
amino acid sequences, a scoring matrix is used to calculate the cumulative score.

Extension of the word hits in each direction are halted when the cumulative alignment score falls off by the quantity X from its maximum achieved value, the cumulative score goes to zero or below due to the accumulation of one or more negative-scoring residue alignments, or the end of either sequence is reached.

- 5 The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength W=11, an expectation E=10, a cutoff of 100, M=5, N=4, and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength (W) of 3, an expectation (E) of 10, and the
10 BLOSUM62 scoring matrix. See Henikoff & Henikoff, (1989) *Proc Natl Acad Sci U.S.A.* 89: 10915.

- In addition to calculating percent sequence identity, the BLAST algorithm also performs a statistical analysis of the similarity between two sequences. See, e.g., Karlin and Altschul, (1993) *Proc Natl Acad Sci U.S.A.* 90: 5873-5887. One
15 measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a test nucleic acid sequence is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid
20 sequence to the reference nucleic acid sequence is less than about 0.1, more preferably less than about 0.01, and most preferably less than about 0.001.

- Percent identity or percent similarity of a DNA or peptide sequence can be determined, for example, by comparing sequence information using the GAP computer program, available from the University of Wisconsin Geneticist
25 Computer Group. The GAP program utilizes the alignment method of Needleman et al., (1970) *J. Mol. Biol.* 48: 443, as revised by Smith et al., (1981) *Adv. Appl. Math.* 2:482. Briefly, the GAP program defines similarity as the number of aligned symbols (i.e., nucleotides or amino acids) which are similar, divided by the total number of symbols in the shorter of the two sequences. The preferred
30 parameters for the GAP program are the default parameters, which do not impose a penalty for end gaps. See, e.g., Schwartz et al., eds., (1979), Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, pp. 357-358, and Gribskov et al., (1986) *Nucl. Acids. Res.* 14: 6745.

The term "similarity" is contrasted with the term "identity". Similarity is defined as above; "identity", however, means a nucleic acid or amino acid sequence having the same amino acid at the same relative position in a given family member of a gene family. Homology and similarity are generally viewed as
5 broader terms than the term identity. Biochemically similar amino acids, for example leucine/isoleucine or glutamate/aspartate, can be present at the same position—these are not identical per se, but are biochemically "similar." As disclosed herein, these are referred to as conservative differences or conservative substitutions. This differs from a conservative mutation at the DNA level, which
10 changes the nucleotide sequence without making a change in the encoded amino acid, e.g. TCC to TCA, both of which encode serine.

As used herein, DNA analog sequences are "substantially identical" to specific DNA sequences disclosed herein if: (a) the DNA analog sequence is derived from coding regions of the nucleic acid sequence shown in any one of odd
15 numbered SEQ ID NOs:1-15 or (b) the DNA analog sequence is capable of hybridization with DNA sequences of (a) under stringent conditions and which encode a biologically active GR α or GR α LBD gene product; or (c) the DNA sequences are degenerate as a result of alternative genetic code to the DNA analog sequences defined in (a) and/or (b). Substantially identical analog proteins
20 and nucleic acids will have between about 70% and 80%, preferably between about 81% to about 90% or even more preferably between about 91% and 99% sequence identity with the corresponding sequence of the native protein or nucleic acid. Sequences having lesser degrees of identity but comparable biological activity are considered to be equivalents.

25 As used herein, "stringent conditions" means conditions of high stringency, for example 6X SSC, 0.2% polyvinylpyrrolidone, 0.2% Ficoll, 0.2% bovine serum albumin, 0.1% sodium dodecyl sulfate, 100 μ g/ml salmon sperm DNA and 15% formamide at 68°C. For the purposes of specifying additional conditions of high stringency, preferred conditions are salt concentration of about 200 mM and
30 temperature of about 45°C. One example of such stringent conditions is hybridization at 4X SSC, at 65°C, followed by a washing in 0.1XSSC at 65°C for one hour. Another exemplary stringent hybridization scheme uses 50% formamide, 4X SSC at 42°C.

In contrast, nucleic acids having sequence similarity are detected by hybridization under lower stringency conditions. Thus, sequence identity can be determined by hybridization under lower stringency conditions, for example, at 50°C or higher and 0.1X SSC (9 mM NaCl/0.9 mM sodium citrate) and the sequences will remain bound when subjected to washing at 55°C in 1X SSC.

As used herein, the term "complementary sequences" means nucleic acid sequences that are base-paired according to the standard Watson-Crick complementarity rules. The present invention also encompasses the use of nucleotide segments that are complementary to the sequences of the present invention.

Hybridization can also be used for assessing complementary sequences and/or isolating complementary nucleotide sequences. As discussed above, nucleic acid hybridization will be affected by such conditions as salt concentration, temperature, or organic solvents, in addition to the base composition, length of the complementary strands, and the number of nucleotide base mismatches between the hybridizing nucleic acids, as will be readily appreciated by those skilled in the art. Stringent temperature conditions will generally include temperatures in excess of about 30°C, typically in excess of about 37°C, and preferably in excess of about 45°C. Stringent salt conditions will ordinarily be less than about 1,000 mM, typically less than about 500 mM, and preferably less than about 200 mM. However, the combination of parameters is much more important than the measure of any single parameter. See, e.g., Wetmur & Davidson, (1968) *J. Mol. Biol.* 31: 349-70. Determining appropriate hybridization conditions to identify and/or isolate sequences containing high levels of homology is well known in the art. See, e.g., Sambrook et al., (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor, New York.

X.D.2. Functional Equivalents of an Engineered NR, SR or GR or NR, SR, GR LBD Mutant Nucleic Acid Sequence of the Present Invention

As used herein, the term "functionally equivalent codon" is used to refer to codons that encode the same amino acid, such as the ACG and AGU codons for serine. For example, GR α or GR α LBD-encoding nucleic acid sequences

comprising any one of odd numbered SEQ ID NOs:1-15, which have functionally equivalent codons are covered by the present invention. Thus, when referring to the sequence example presented in odd numbered SEQ ID NOs:1-15, applicants provide substitution of functionally equivalent codons into the sequence example
5 of in odd numbered SEQ ID NOs:1-15. Thus, applicants are in possession of amino acid and nucleic acids sequences which include such substitutions but which are not set forth herein in their entirety for convenience.

It will also be understood by those of skill in the art that amino acid and nucleic acid sequences can include additional residues, such as additional N- or
10 C-terminal amino acids or 5' or 3' nucleic acid sequences, and yet still be essentially as set forth in one of the sequences disclosed herein, so long as the sequence retains biological protein activity where polypeptide expression is concerned. The addition of terminal sequences particularly applies to nucleic acid sequences which can, for example, include various non-coding sequences
15 flanking either of the 5' or 3' portions of the coding region or can include various internal sequences, i.e., introns, which are known to occur within genes.

X.D.3. Biological Equivalents

The present invention envisions and includes biological equivalents of a
20 engineered NR, SR or GR or NR, SR or GR LBD mutant polypeptide of the present invention. The term "biological equivalent" refers to proteins having amino acid sequences which are substantially identical to the amino acid sequence of an engineered NR, SR or GR LBD mutant of the present invention and which are capable of exerting a biological effect in that they are capable of binding small
25 molecules or cross-reacting with anti- NR, SR or GR or NR, SR or GR LBD mutant antibodies raised against an engineered mutant NR, SR or GR or NR, SR or GR LBD polypeptide of the present invention.

For example, certain amino acids can be substituted for other amino acids in a protein structure without appreciable loss of interactive capacity with, for
30 example, structures in the nucleus of a cell. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence substitutions can be made in a protein sequence (or the nucleic acid sequence encoding it) to obtain a protein with the same, enhanced, or

antagonistic properties. Such properties can be achieved by interaction with the normal targets of the protein, but this need not be the case, and the biological activity of the invention is not limited to a particular mechanism of action. It is thus in accordance with the present invention that various changes can be made in the amino acid sequence of an engineered NR, SR or GR or NR, SR or GR LBD mutant polypeptide of the present invention or its underlying nucleic acid sequence without appreciable loss of biological utility or activity.

Biologically equivalent polypeptides, as used herein, are polypeptides in which certain, but not most or all, of the amino acids can be substituted. Thus, when referring to the sequence examples presented in any of even numbered SEQ ID NOs:2-16, applicants envision substitution of codons that encode biologically equivalent amino acids, as described herein, into a sequence example of even numbered SEQ ID NOs: 2-16, respectively. Thus, applicants are in possession of amino acid and nucleic acids sequences which include such substitutions but which are not set forth herein in their entirety for convenience.

Alternatively, functionally equivalent proteins or peptides can be created via the application of recombinant DNA technology, in which changes in the protein structure can be engineered, based on considerations of the properties of the amino acids being exchanged, e.g. substitution of Ile for Leu. Changes designed by man can be introduced through the application of site-directed mutagenesis techniques, e.g., to introduce improvements to the antigenicity of the protein or to test an engineered mutant polypeptide of the present invention in order to modulate lipid-binding or other activity, at the molecular level.

Amino acid substitutions, such as those which might be employed in modifying an engineered mutant polypeptide of the present invention are generally, but not necessarily, based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. An analysis of the size, shape and type of the amino acid side-chain substituents reveals that arginine, lysine and histidine are all positively charged residues; that alanine, glycine and serine are all of similar size; and that phenylalanine, tryptophan and tyrosine all have a generally similar shape. Therefore, based upon these considerations, arginine, lysine and histidine; alanine, glycine and serine; and phenylalanine, tryptophan and tyrosine; are

defined herein as biologically functional equivalents. Those of skill in the art will appreciate other biologically functionally equivalent changes. It is implicit in the above discussion, however, that one of skill in the art can appreciate that a radical, rather than a conservative substitution is warranted in a given situation.

5 Non-conservative substitutions in engineered mutant LBD polypeptides of the present invention are also an aspect of the present invention.

In making biologically functional equivalent amino acid substitutions, the hydrophobic index of amino acids can be considered. Each amino acid has been assigned a hydrophobic index on the basis of their hydrophobicity and charge characteristics, these are: isoleucine (+ 4.5); valine (+ 4.2); leucine (+ 3.8);
10 phenylalanine (+ 2.8); cysteine (+ 2.5); methionine (+ 1.9); alanine (+ 1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5); glutamine (-3.5); aspartate (-3.5); asparagine (-3.5); lysine (-3.9); and arginine (-4.5).

15 The importance of the hydrophobic amino acid index in conferring interactive biological function on a protein is generally understood in the art (Kyte & Doolittle, (1982), *J. Mol. Biol.* 157: 105-132, incorporated herein by reference). It is known that certain amino acids can be substituted for other amino acids having a similar hydrophobic index or score and still retain a similar biological
20 activity. In making changes based upon the hydrophobic index, the substitution of amino acids whose hydrophobic indices are within ± 2 of the original value is preferred, those which are within ± 1 of the original value are particularly preferred, and those within ± 0.5 of the original value are even more particularly preferred.

It is also understood in the art that the substitution of like amino acids can
25 be made effectively on the basis of hydrophilicity. U.S. Patent No. 4,554,101, incorporated herein by reference, states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with its immunogenicity and antigenicity, i.e. with a biological property of the protein. It is understood that an amino acid can be substituted for
30 another having a similar hydrophilicity value and still obtain a biologically equivalent protein.

As detailed in U.S. Patent No. 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+ 3.0); lysine (+ 3.0);

aspartate (+ 3.0 \pm 1); glutamate (+ 3.0 \pm 1); serine (+ 0.3); asparagine (+ 0.2); glutamine (+ 0.2); glycine (0); threonine (-0.4); proline (-0.5 \pm 1); alanine (-0.5); histidine (-0.5); cysteine (-1.0); methionine (-1.3); valine (-1.5); leucine (-1.8); isoleucine (-1.8); tyrosine (-2.3); phenylalanine (-2.5); tryptophan (-3.4).

5 In making changes based upon similar hydrophilicity values, the substitution of amino acids whose hydrophilicity values are within ± 2 of the original value is preferred, those which are within ± 1 of the original value are particularly preferred, and those within ± 0.5 of the original value are even more particularly preferred.

10 While discussion has focused on functionally equivalent polypeptides arising from amino acid changes, it will be appreciated that these changes can be effected by alteration of the encoding DNA, taking into consideration also that the genetic code is degenerate and that two or more codons can code for the same amino acid.

15 Thus, it will also be understood that this invention is not limited to the particular amino acid and nucleic acid sequences of any of SEQ ID NOs:1-16. Recombinant vectors and isolated DNA segments can therefore variously include an engineered NR, SR or GR or NR, SR or GR LBD mutant polypeptide-encoding region itself, include coding regions bearing selected alterations or modifications
20 in the basic coding region, or include larger polypeptides which nevertheless comprise an NR, SR or GR or NR, SR or GR LBD mutant polypeptide-encoding regions or can encode biologically functional equivalent proteins or polypeptides which have variant amino acid sequences. Biological activity of an engineered NR, SR or GR or NR, SR or GR LBD mutant polypeptide can be determined, for
25 example, by transcription assays known to those of skill in the art.

The nucleic acid segments of the present invention, regardless of the length of the coding sequence itself, can be combined with other DNA sequences, such as promoters, enhancers, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such
30 that their overall length can vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length can be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, nucleic acid fragments can be prepared

which include a short stretch complementary to a nucleic acid sequence set forth in any of odd numbered SEQ ID NOs:1-15, such as about 10 nucleotides, and which are up to 10,000 or 5,000 base pairs in length. DNA segments with total lengths of about 4,000, 3,000, 2,000, 1,000, 500, 200, 100, and about 50 base pairs in length are also useful.

The DNA segments of the present invention encompass biologically functional equivalents of engineered NR, SR or GR, or NR, SR or GR LBD mutant polypeptides. Such sequences can arise as a consequence of codon redundancy and functional equivalency that are known to occur naturally within nucleic acid sequences and the proteins thus encoded. Alternatively, functionally equivalent proteins or polypeptides can be created via the application of recombinant DNA technology, in which changes in the protein structure can be engineered, based on considerations of the properties of the amino acids being exchanged. Changes can be introduced through the application of site-directed mutagenesis techniques, e.g., to introduce improvements to the antigenicity of the protein or to test variants of an engineered mutant of the present invention in order to examine the degree of binding activity, or other activity at the molecular level. Various site-directed mutagenesis techniques are known to those of skill in the art and can be employed in the present invention.

The invention further encompasses fusion proteins and peptides wherein an engineered mutant coding region of the present invention is aligned within the same expression unit with other proteins or peptides having desired functions, such as for purification or immunodetection purposes.

Recombinant vectors form important further aspects of the present invention. Particularly useful vectors are those in which the coding portion of the DNA segment is positioned under the control of a promoter. The promoter can be that naturally associated with an NR, SR or GR gene, as can be obtained by isolating the 5' non-coding sequences located upstream of the coding segment or exon, for example, using recombinant cloning and/or PCR technology and/or other methods known in the art, in conjunction with the compositions disclosed herein.

In other embodiments, certain advantages will be gained by positioning the coding DNA segment under the control of a recombinant, or heterologous, promoter. As used herein, a recombinant or heterologous promoter is a promoter

that is not normally associated with an NR, SR or GR gene in its natural environment. Such promoters can include promoters isolated from bacterial, viral, eukaryotic, or mammalian cells. Naturally, it will be important to employ a promoter that effectively directs the expression of the DNA segment in the cell type chosen for expression. The use of promoter and cell type combinations for protein expression is generally known to those of skill in the art of molecular biology (See, e.g., Sambrook et al., (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York, specifically incorporated herein by reference). The promoters employed can be constitutive or inducible and can be used under the appropriate conditions to direct high level expression of the introduced DNA segment, such as is advantageous in the large-scale production of recombinant proteins or peptides. One preferred promoter system contemplated for use in high-level expression is a T7 promoter-based system.

15 X.E. Antibodies to an Engineered NR, SR or GR or NR, SR, GR LBD Mutant Polypeptide of the Present Invention

The present invention also provides an antibody that specifically binds a engineered NR, SR or GR or NR, SR, GR LBD mutant polypeptide and methods to generate same. The term "antibody" indicates an immunoglobulin protein, or functional portion thereof, including a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a single chain antibody, Fab fragments, and a Fab expression library. "Functional portion" refers to the part of the protein that binds a molecule of interest. In a preferred embodiment, an antibody of the invention is a monoclonal antibody. Techniques for preparing and characterizing antibodies are well known in the art (See, e.g., Harlow & Lane (1988) Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). A monoclonal antibody of the present invention can be readily prepared through use of well-known techniques such as the hybridoma techniques exemplified in U.S. Patent No 4,196,265 and the phage-displayed techniques disclosed in U.S. Patent No. 5,260,203.

30 The phrase "specifically (or selectively) binds to an antibody", or "specifically (or selectively) immunoreactive with", when referring to a protein or peptide, refers to a binding reaction which is determinative of the presence of the

protein in a heterogeneous population of proteins and other biological materials. Thus, under designated immunoassay conditions, the specified antibodies bind to a particular protein and do not show significant binding to other proteins present in the sample. Specific binding to an antibody under such conditions can require an
5 antibody that is selected for its specificity for a particular protein. For example, antibodies raised to a protein with an amino acid sequence encoded by any of the nucleic acid sequences of the invention can be selected to obtain antibodies specifically immunoreactive with that protein and not with unrelated proteins.

The use of a molecular cloning approach to generate antibodies,
10 particularly monoclonal antibodies, and more particularly single chain monoclonal antibodies, are also provided. The production of single chain antibodies has been described in the art. See, e.g., U.S. Patent No. 5,260,203. For this approach, combinatorial immunoglobulin phagemid libraries are prepared from RNA isolated from the spleen of the immunized animal, and phagemids expressing appropriate
15 antibodies are selected by panning on endothelial tissue. The advantages of this approach over conventional hybridoma techniques are that approximately 10^4 times as many antibodies can be produced and screened in a single round, and that new specificities are generated by heavy (H) and light (L) chain combinations in a single chain, which further increases the chance of finding appropriate
20 antibodies. Thus, an antibody of the present invention, or a "derivative" of an antibody of the present invention, pertains to a single polypeptide chain binding molecule which has binding specificity and affinity substantially similar to the binding specificity and affinity of the light and heavy chain aggregate variable region of an antibody described herein.

25 The term "immunochemical reaction", as used herein, refers to any of a variety of immunoassay formats used to detect antibodies specifically bound to a particular protein, including but not limited to competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric
30 assays, gel diffusion precipitation reactions, immunodiffusion assays, *in situ* immunoassays (e.g., using colloidal gold, enzyme or radioisotope labels), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence

assays, protein A assays, and immunoelectrophoresis assays, etc. See Harlow & Lane (1988) for a description of immunoassay formats and conditions.

5 X.F. Method for Detecting an Engineered NR, SR or GR or NR, SR, GR
 LBD Mutant Polypeptide or an Nucleic Acid Molecule Encoding the
 Same

 In another aspect of the invention, a method is provided for detecting a level of an engineered NR, SR or GR or NR, SR, GR LBD mutant polypeptide using an antibody that specifically recognizes an engineered NR, SR or GR or
10 NR, SR, GR LBD mutant polypeptide, or portion thereof. In a preferred embodiment, biological samples from an experimental subject and a control subject are obtained, and an engineered NR, SR or GR or NR, SR, GR LBD mutant polypeptide is detected in each sample by immunochemical reaction with the antibody. More preferably, the antibody recognizes amino acids of any one of
15 the even-numbered SEQ ID NOs:4, 6, 8, 12, 14, and 16, and is prepared according to a method of the present invention for producing such an antibody.

 In one embodiment, an antibody is used to screen a biological sample for the presence of an engineered NR, SR or GR or NR, SR, GR LBD mutant polypeptide. A biological sample to be screened can be a biological fluid such as
20 extracellular or intracellular fluid, or a cell or tissue extract or homogenate. A biological sample can also be an isolated cell (e.g., in culture) or a collection of cells such as in a tissue sample or histology sample. A tissue sample can be suspended in a liquid medium or fixed onto a solid support such as a microscope slide. In accordance with a screening assay method, a biological sample is
25 exposed to an antibody immunoreactive with an engineered NR, SR or GR or NR, SR, GR LBD mutant polypeptide whose presence is being assayed, and the formation of antibody-polypeptide complexes is detected. Techniques for detecting such antibody-antigen conjugates or complexes are well known in the art and include but are not limited to centrifugation, affinity chromatography and
30 the like, and binding of a labeled secondary antibody to the antibody-candidate receptor complex.

 In another aspect of the invention, a method is provided for detecting a nucleic acid molecule that encodes an engineered NR, SR or GR or NR, SR, GR

LBD mutant polypeptide. According to the method, a biological sample having nucleic acid material is procured and hybridized under stringent hybridization conditions to an engineered NR, SR or GR or NR, SR, GR LBD mutant polypeptide-encoding nucleic acid molecule of the present invention. Such hybridization enables a nucleic acid molecule of the biological sample and an engineered NR, SR or GR or NR, SR, GR LBD mutant polypeptide encoding-nucleic acid molecule to form a detectable duplex structure. Preferably, the an engineered NR, SR or GR or NR, SR, GR LBD mutant polypeptide encoding-nucleic acid molecule includes some or all nucleotides of any one of the odd-numbered SEQ ID NOs:3, 5, 7, 11, 13, and 15. Also preferably, the biological sample comprises human nucleic acid material.

XI. The Role of the Three-Dimensional Structure of the GR α LBD in Solving Additional NR, SR or GR Crystals

Because polypeptides can crystallize in more than one crystal form, the structural coordinates of a GR α LBD, or portions thereof, as provided by the present invention, are particularly useful in solving the structure of other crystal forms of GR α and the crystalline forms of other NRs, SRs and GRs. The coordinates provided in the present invention can also be used to solve the structure of NR, SR or GR and NR, SR or GR LBD mutants (such as those described in Sections IX and X above), NR, SR or GR LBD co-complexes, or of the crystalline form of any other protein with significant amino acid sequence homology to any functional domain of NR, SR or GR.

XI.A. Determining the Three-Dimensional Structure of a Polypeptide Using the Three-Dimensional Structure of the GR α LBD as a Template in Molecular Replacement

One method that can be employed for the purpose of solving additional GR crystal structures is molecular replacement. See generally, Rossmann, ed, (1972) The Molecular Replacement Method, Gordon & Breach, New York. In the molecular replacement method, the unknown crystal structure, whether it is another crystal form of a GR α or a GR α LBD, (i.e. a GR α or a GR α LBD mutant), or an NR, SR or GR or an NR, SR or GR LBD polypeptide complexed with

another compound (a "co-complex"), or the crystal of some other protein with significant amino acid sequence homology to any functional region of the GR α LBD, can be determined using the GR α LBD structure coordinates provided in Table 4. This method provides an accurate structural form for the unknown
5 crystal more quickly and efficiently than attempting to determine such information *ab initio*.

In addition, in accordance with this invention, NR, SR or GR and NR, SR or GR LBD mutants can be crystallized in complex with known modulators. The crystal structures of a series of such complexes can then be solved by molecular
10 replacement and compared with that of the wild-type NR, SR or GR or the wild-type NR, SR or GR LBD. Potential sites for modification within the various binding sites of the enzyme can thus be identified. This information provides an additional tool for determining the most efficient binding interactions, for example, increased hydrophobic interactions, between the GR α LBD and a chemical entity
15 or compound.

All of the complexes referred to in the present disclosure can be studied using X-ray diffraction techniques (See, e.g., Blundell & Johnson (1985) Method.Enzymol., 114A & 115B, (Wyckoff et al., eds.), Academic Press; McRee, (1993) Practical Protein Crystallography, Academic Press, New York) and can be
20 refined using computer software, such as the X-PLOR™ program (Brünger, (1992) X-PLOR, Version 3.1. A System for X-ray Crystallography and NMR, Yale University Press, New Haven, Connecticut; X-PLOR is available from Molecular Simulations, Inc., San Diego, California) and the XTAL-VIEW program (McRee, (1992) J. Mol. Graphics 10: 44-46; McRee, (1993) Practical Protein
25 Crystallography, Academic Press, San Diego, California). This information can thus be used to optimize known classes of GR and GR LBD modulators, and more importantly, to design and synthesize novel classes of GR and GR LBD modulators.

30

Laboratory Examples

The following Laboratory Examples have been included to illustrate preferred modes of the invention. Certain aspects of the following Laboratory Examples are described in terms of techniques and procedures found or

contemplated by the present inventors to work well in the practice of the invention. These Laboratory Examples are exemplified through the use of standard laboratory practices of the inventors. In light of the present disclosure and the general level of skill in the art, those of skill will appreciate that the following

5 Laboratory Examples are intended to be exemplary only and that numerous changes, modifications and alterations can be employed without departing from the spirit and scope of the invention.

Example 1

10 Construction of the Modified pET24 Expression Vector

The expression vector pGEX-2T (Amersham Pharmacia Biotech, Piscataway, New Jersey) was used as a template in a polymerase chain reaction to engineer a polyhistidine tag in frame to the sequence encoding glutathione S-transferase (GST) and a thrombin protease site. The forward primer contained a

15 Nde I site (5' CGG CGG CGC CAT ATG AAA AAA GGT (CAT)₆ GGT TCC CCT ATA CTA GGT TAT TGG A 3') (SEQ ID NO:19) and the reverse primer (5' CGG CGG CGC GGA TCC ACG CGG AAC CAG ATC CGA 3') (SEQ ID NO:20) contained a BamH I site which allowed for direct cloning of the amplified product into pET24a (Novagen, Inc., Madison, Wisconsin) following restriction enzyme

20 digestion. The resulting sequence of the modified GST (SEQ ID NO:21)(last six residues are thrombin protease site) is below:

MKKGHHHHH HGSPILGYWK IKGLVQPTL LLEYLEEKYE EHLIERDEGD 50
 KWRNKKFELG LEFPNLPYYI DGDVKLTQSM AIIRYIADKH NMLGGCPKER 100
 AEISMLEGAV LDIRYGVSRI AYSKDFETLK VDFLSKLPEM LKMFEDRLCH 150
 25 KTYLNGDHVT HPDFMLYDAL DVVLYMDPMC LDAFPKLVCF KKRIEAIPQI 200
 DKYLKSSKYI AWPLQGWQAT FGGGDHPPKS DLVPRGS 237

Example 2

30 Mutagenesis (F602S AND F602D) of Human GR Ligand Binding Domain (LBD)

Two complimentary oligonucleotides for each desired mutation were constructed. The following sequences represent the oligonucleotides for the Phenylalanine 602 Serine mutation:

-101-

Forward Primer (F602S) (SEQ ID NO:22):

5' TAC TCC TGG ATG TCC CTT ATG GCA TTT GCT CT 3'

Reverse Primer (F602S) (SEQ ID NO:23):

5' AG AGC AAA TGC CAT AAG GGA CAT CCA GGA GTA 3'

Another separate mutation was also constructed. The sequences below represent the oligonucleotides for the Phenylalanine 602 Aspartic Acid mutation:

Forward Primer (F602D) (SEQ ID NO:24):

5' TAC TCC TGG ATG GAC CTT ATG GCA TTT GCT CT 3'

Reverse Primer (F602D) (SEQ ID NO:25):

5' AG AGC AAA TGC CAT AAG GTC CAT CCA GGA GTA 3'

The underlined letters depict the base changes from the wild type human GR sequence. The GR LBD (amino acids 521-777) (SEQ ID NOs:9-10) previously cloned into the pRSET A vector (Invitrogen of Carlsbad, California) was used as the backbone to create the mutants. The procedure used to make the mutation is outlined in the QuickChange Site-Directed Mutagenesis Kit sold by Stratagene, La Jolla, California (Catalog # 200518). After the constructs were sequence verified, the mutants of GR-LBD were subcloned inframe with the glutathione S-transferase in the modified pET24 expression vector. A thrombin protease site at the C-terminus of the glutathione S-transferase allows for cleavage of the resultant fusion protein following expression.

The resulting final amino acid sequences for the mutant GR LBDs are below. The underlined, bolded amino acids depict the changes from the wild type human GR sequence.

GR-LBD(521-777) F602S (SEQ ID NO:12)

VPATLPQLTP TLVSLLEVIE PEVLYAGYDS SVPDSTWRIM TTLNMLGGRQ
VIAAVKWAKA IPGFRNLHLD DQMTLLQYSW **MS**LMFAFGW RSYRQSSANL
LCFAPDLIIN EQRMTLPCMY DQCKHMLYVS SELHRLQVSY EEYLCMKTLL

-102-

LLSSVPKDGL KSQELFDEIR MTYIKELGKA IVKREGNSSQ NWQRFYQLTK
 LLDSMHEVVE NLLNYCFQTF LDKTMSIEFP EMLAEIITNQ IPKYSNGNIK
 KLLFHQK

5

GR-LBD(521-777) F602D (SEQ ID NO:14)

VPATLPQLTP TLVSLLEVIE PEVLYAGYDS SVPDSTWRIM TTLNMLGGRQ
 VIAAVKWAKA IPGFRNLHLD DQMTLLQYSW MDLMAFALGW RSYRQSSANL
 10 LCFAPDLIIN EQRMTLPCMY DQCKHMLYVS SELHRLQVSY EEYLCMKTLL
 LLSSVPKDGL KSQELFDEIR MTYIKELGKA IVKREGNSSQ NWQRFYQLTK
 LLDSMHEVVE NLLNYCFQTF LDKTMSIEFP EMLAEIITNQ IPKYSNGNIK
 KLLFHQK

15

Example 3

Expression of the Fusion Protein

BL21(DE3) cells (Novagen, Inc., Madison, Wisconsin) were transformed following established protocols. Following overnight incubation at 37°C a single colony was used to inoculate a 10 ml LB culture containing 50 µg/ml kanamycin (Sigma Chemical Company, St. Louis, Missouri). The culture was grown for ~12 hrs at 37°C and then a 500µl aliquot was used to inoculate flasks containing 1 liter Circle Grow media (Bio101, Inc., now Qbiogene of Carlsbad, California) and the required antibiotic. The cells were then grown at 22°C to an OD600 between 1 and 2 and then cooled to 16°C. Following a 30 min equilibration at that temperature, dexamethasone (Spectrum, Gardena, California) (10 µM final concentration) was added. Induction of expression was achieved by adding IPTG (BACHEM AG, Switzerland) (final concentration 1 mM) to the cultures. Expression at 16°C was continued for ~ 24 hrs. Cells were then harvested and frozen at -80°C.

30

Referring now to Figure 1A, *E. coli* expression of mutant 6xHisGST-GR(521-777) F602S is shown. Shown are the pellet (P - insoluble) and eluent (E - soluble Ni⁺⁺ binding) fractions of protein expressed in the absence of ligand (NL - lanes 2 and 3) or in the presence (10 micromolar) of dexamethasone (DEX),

lanes 4 and 5, or RU486, lanes 6 and 7. The positions of molecular mass (kDa) markers M (lane 1) (94, 67, 43, 30, 20 and 14 kDa, respectively) and of the expressed protein are indicated to the left and right sides of the panel, respectively.

5 Referring now to Figure 1B, *E coli* expression of mutant 6xHisGST-GR(521-777) F602D is shown. Shown are eluent fractions from Ni⁺⁺ chelated resin of two separate samples. Protein was expressed in either the presence (+, lanes 2 and 4, 10 micromolar) or absence (-, lanes 3 and 5) of dexamethasone. The positions of molecular mass (kDa) markers M (lane 1) (94, 67, 43, 30, 20 and
10 14 kDa, respectively) and of the expressed protein are indicated to the left and right sides of the panel, respectively.

Example 4

Purification Of GR-LBD (F602S)

15 ~200 g cells were resuspended in 700mL lysis buffer (50mM Tris pH =8.0, 150 mM NaCl, 2M Urea, 10% glycerol and 100 μ M dexamethasone) and lysed by passing 3 times through an APV Lab 2000 homogenizer. The lysate was subjected to centrifugation (45 minutes, 20,000g, 4°C), followed by a second 20 min spin at 20,000 g, 4°. The cleared supernatant was filtered through coarse pre-
20 filters and 50 mM Tris, pH= 8.0, containing 150 mM NaCl, 10% glycerol and 1M imidazole was added to obtain a final imidazole concentration of 50mM. This lysate was loaded onto a XK-26 column (Pharmacia, Peapack, New Jersey) packed with SEPHAROSE® [Ni⁺⁺ charged] Chelation resin (Pharmacia, Peapack, New Jersey) and pre-equilibrated with lysis buffer supplemented with 50mM
25 imidazole. Following loading, the column was washed to baseline absorbance with equilibration buffer and a linear urea gradient (2M to 0). For elution the column was developed with a linear gradient from 50 to 500 mM Imidazole in 50mM Tris pH =8.0, 150 mM NaCl, 10% glycerol and 30 μ M dexamethasone. Column fractions of interest were pooled and 500 units of thrombin protease
30 (Amersham Pharmacia Biotech, Piscataway, New Jersey) were added for the cleavage of the fusion protein.

This solution was then dialyzed against 1 liter of 50 mM Tris pH =8.0, 150 mM NaCl, 10% glycerol and 20 μ M dexamethasone for ~10 hrs at 4°C. The

digested protein sample was filtered and then reloaded onto the same re-equilibrated column. The cleaved GR-LBD was collected in the flow through fraction. The diluted protein sample was concentrated with Centri-prep™ 10K centrifugal filtration devices (Amicon/Millipore, Bedford, Massachusetts) to a volume of 30mls and then diluted 5 fold with 50 mM Tris pH=8.0, 10 % glycerol, 10 mM DTT, 0.5 mM EDTA and 30 µM dexamethasone. The sample was then loaded onto a pre-equilibrated XK-26 column (Pharmacia, Peapack, New Jersey) packed with Poros HQ resin (PerSeptive Biosystems, Framingham, Massachusetts). The cleaved GR LBD was collected in the flowthrough. The NaCl concentration was adjusted to 500mM and the dexamethasone concentration was adjusted to 50 µM before the purified protein was concentrated to ~1 mg/ml using the Centri-prep™ 10K centrifugal filtration devices.

Figure 1A depicts purification of *E. coli* expressed GR(521-777) F602S by SDS-PAGE. Lane 1 contains the insoluble pellet fraction. Lane 2 contains the soluble supernatant fraction. Lane 3 contains pooled eluent from initial Ni⁺⁺ column. Lane 4 contains the sample after thrombin digestion. Lane 5 contains the flow through fraction after reload of the Ni⁺⁺ column. Lane 6 contains the concentrated protein after anion exchange. The positions of molecular mass (kDa) markers (in Lane M, 94, 67, 43, 30, 20 and 14 kDa, respectively) and of the expressed protein are indicated to the left and right sides of the panel, respectively. Purification provides for the removal of any remaining associated bacterial HSPs.

The final resultant sequence (SEQ ID NO:32) of the purified protein is below. The first two residues (underlined and bolded) are vector derived and represent the remaining residues of the thrombin cleavage site following digestion.

GSVPATLPQL TPTLVSLLEV IEPEVLYAGY DSSVPDSTWR IMTTLNMLGG
 RQVIAAVKWA KAIPGFRNLH LDDQMTLLQY SWMSLMAFAL GWRSYRQSSA
 NLLCFAPDLI INEQRM TLPC MYDQCKHMLY VSSELHRLQV SYEEYLCMKT
 LLLSSV PKD GLKSQELFDE IRMTYIKELG KAIVKREGNS SQNWQRFYQL
 TKLLDSMHEV VENLLNYCFQ TFLDKTMSIE FPEMLAEIIT NQIPKYSNGN
 IKKLLFHQK

Example 5Ligand and Coactivator Binding Of GR

All experiments were conducted with buffer containing 10 mM HEPES pH 7.4, 0.15 M NaCl, 3 mM EDTA, 0.005% polysorbate-20 and 5 mM DTT. For activity determinations, 10 nM of fluorescein dexamethasone (Molecular Probes, Eugene, Oregon) was titrated with increasing concentrations of the glucocorticoid receptor in black 96-well plates (CoStar, Cambridge, Massachusetts). The fluorescence polarization values for each concentration of receptor were determined using a BMG PolarStar Galaxy fluorescence plate reader (BMG Labtechnologies GmbH, Offenburg, Germany) with 485 nm excitation and 520 nm emission filters. Binding isotherms were constructed and apparent EC50 values were determined by non-linear least squares fit of the data to an equation for a simple 1:1 interaction. Note that these EC50 values are not corrected for the unlabeled dexamethasone present in the GR receptor preparations. For stability studies, the fluorescent polarization of 10 nM fluorescein dexamethasone with 1 μ M GST-GR LBD 521-777 (F602S) is read at specific time intervals in the presence or absence of 25 μ M of a peptide derived from the coactivator TIF2. (TIF2 732-756: QEPVSPKKKENALLRYLLDKDDTKD) (SEQ ID NO:17).

Data from these experiments are presented graphically in Figures 2A-2C. These studies demonstrate that the GST-GR fusion protein and the cleaved GR LBD alone bind dexamethasone in a saturable and competitive manner (Figure 2A). It was also found that the GST-GR fusion protein binds a peptide from the coactivator TIF2 with a submicromolar affinity. Binding of the GST-GR fusion protein is enhanced by the agonist dexamethasone (DEX) and inhibited by the antagonist RU486 (Fig. 2B). Finally, it was also found that the addition of the TIF2 peptide stabilizes the dexamethasone binding activity of the GST-GR fusion protein.

Figure 2B was generated using Biacore techniques. Biacore relies on changes in the refractive index at the surface layer upon binding of a ligand to a protein immobilized on the layer. In this system, a collection of small ligands is injected sequentially in a 2-5 microliter cell, wherein the protein is immobilized within the cell. Binding is detected by surface plasmon resonance (SPR) by recording laser light refracting from the surface. In general, the refractive index

change for a given change of mass concentration at the surface layer is practically the same for all proteins and peptides, allowing a single method to be applicable for any protein (Liedberg et al. (1983) *Sensors Actuators* 4:299-304; Malmquist (1993) *Nature* 361:186-187). The purified protein is then used in the assay
5 without further preparation. A synthetic peptide with an amino-terminal biotin is coupled to a sensor chip immobilized with streptavidin. The chip thus prepared is then exposed to the potential ligand via the delivery system incorporated in the instruments sold by Biacore (Uppsala, Sweden) to pipet the ligands in a sequential manner (autosampler). The SPR signal on the chip is recorded and
10 changes in the refractive index indicate an interaction between the immobilized target and the ligand. Analysis of the signal kinetics of on rate and off rate allows the discrimination between non-specific and specific interaction.

Example 6

15 Preparation of the GR/TIF2/Dex Complex

The GR/TIF2/Dex complex was prepared by adding a 2-fold excess of a TIF2 peptide containing sequence of QEPVSPKKKENALLRYLLDKDDTKD (SEQ ID NO:17). The above complex was diluted 10 folds with a buffer containing 500 mM ammonium acetate (NH₄OAC), 50 mM Tris, pH 8.0, 10% glycerol, 10 mM
20 dithiothreitol (DTT), 0.5 mM EDTA, and 0.05% beta-N-octoglucoside (b-OG), and was slowly concentrated to 6.3 mg/ml, then aliquoted and stored at -80°C.

Example 7

Crystallization and Data Collection

25 The GR/TIF2/DEX crystals were grown at room temperature in hanging drops containing 3.0 ul of the above protein-ligand solutions, and 0.5 ul of well buffer (50mM HEPES, pH 7.5-8.5 (preferred pH range is 8.0 to 8.5), and 1.7-2.3M ammonium formate). Crystals were also obtained with mixing of the above protein
30 solution and the well buffer at various volume ratios. Crystals appeared overnight and continuously grew to a size up to 300 micron within a week. Before data collection,

crystals were transiently mixed with the well buffer that contained an additional 25 % glycerol, and were then flash frozen in liquid nitrogen.

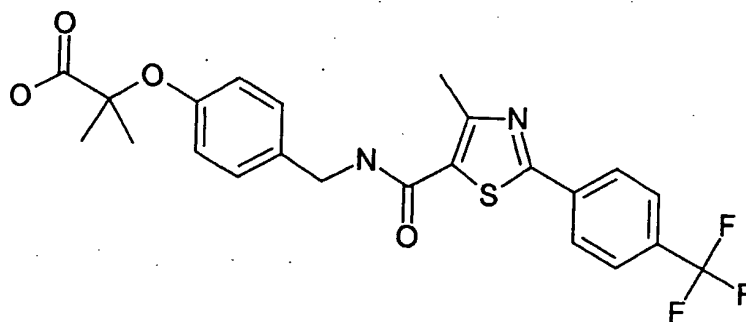
The GR/TIF2/DEX crystals formed in the $P6_1$ space group, with $a = b = 126.014 \text{ \AA}$, $c = 86.312 \text{ \AA}$, $\alpha = \beta = 90^\circ$, and $\gamma = 120^\circ$. Each asymmetry unit contains two molecules of the GR LBD with 56% of solvent content. Data were collected with a Rigaku Raxis IV detector in house. The observed reflections were reduced, merged and scaled with DENZO and SCALEPACK in the HKL2000 package (Z. Otwinowski and W. Minor (1997)).

Example 8

Structure Determination and Refinement

Table 5 is a table of the atomic structure coordinates used as the initial model to solve the structure of the GR/TIF2/dexamethasone complex by molecular replacement. The GR model is a homology model built on the published structure of the progesterone receptor LBD and the SRC1 coactivator peptide from the PPAR α /Compound 1/SRC1 structure.

Compound 1 is an agonist of hPPAR α , and has the IUPAC name 2-methyl-2-[4-[[[(4-methyl-2-[4-trifluoromethylphenyl] thiazol-5-yl-carbonyl) amino] methyl] phenoxy] propionic acid.



Compound 1

The initial model for the molecular replacement calculation comprised coordinates for residues 527-776 of wild-type GR together with coordinates for residues 685-697 of SRC-1, a coactivator very similar to TIF2. The model for GR was built from the crystal structure of PR bound to progesterone (Shawn P. Williams and Paul B. Sigler, *Nature* 393, 392-396 (1998)) using the MVP program

(Lambert, 1997). The coordinates for SRC-1 were obtained from a crystal structure of PPAR α bound to SRC-1. The SRC-1 model was positioned in the coactivator binding site of GR by rotating the GR model and PPAR α /SRC-1 complex into a common orientation that superimposed their backbone atoms.

5 It is noted that the amino acid sequence for SRC-1 differs substantially from that of TIF2, although both coactivator sequences have the LXXLL motif. Model building, including conversion of side-chains from the SRC-1 and wild-type GR sequences to the actual TIF2 and GR F602S sequences, respectively, was carried out with QUANTATM.

10 This model was used in molecular replacement search with the CCP4 AmoReTM program (Collaborative Computational Project Number 4, 1994, "The CCP4 Suite: Programs for Protein Crystallography", *Acta Cryst.* D50, 760-763; J.Navaza, *Acta Cryst.* A50, 157-163 (1994)) to determine the initial structure solutions. Two solutions were obtained from the molecular replacement search
15 with a correlation coefficient of 43% and an R-factor of 45.3%, consistent with two complexes within each asymmetry unit. The calculated phase from the molecular replacement solutions was improved with solvent flattening, histogram matching and the two-fold noncrystallographic averaging as implement in the CCP4 dm program, and produced a clear map for the GR LBD, the TIF2 peptide
20 and the dexamethasone. As noted above, model building proceeded with QUANTATM, and refinement progressed with CNX (Accelrys, Princeton, New Jersey) and multiple cycle of manual rebuilding. The statistics of the structure are summarized in Table 3 and coordinates are presented in Figure 4.

Surface areas calculated with the Connolly MS program (Michael L.
25 Connolly, "Solvent-Accessible Surfaces of Proteins and Nucleic Acids," *Science* 221, 709-713 (1983)) and the MVP program (Lambert, 1997). The pocket volume and binding site accessible waters were calculated with MVP.

Example 9

30 Random Mutant Library of GR LBD and Selection using the LacI Fusion System

The expression vector pJS142A (Affymax Inc., Palo Alto, California) containing the LacI protein was used to clone the wild type GR LBD in frame with the LacI gene. Using standard error-incorporating PCR techniques, a random

mutant library was created within the context of the GR LBD. An advantage of the LacI expression system is that the protein expressed has the ability to bind the plasmid DNA from which it was derived. The mutant fusion proteins produced by the random library were expressed in *E. Coli* at 37°C. Lysis of the cell cultures was achieved using lysozyme. The cell lysates were then added to a microtiter plate containing the immobilized coactivator peptide biotinylated-TIF2 NR BoxIII. The plasmid DNA was eluted from the DNA-protein complex bound to the plate using 1mM IPTG (Life Technologies). The eluted DNA was then re-transformed and individual clones were isolated for sequence analysis. Mutant fusion proteins with increased solubility and activity (ability to bind coactivator) should be selected for after rounds of panning and increased stringency washes. Once the sequence of the mutant LacI-GR LBD was identified, the same mutation was also made in the pET24 expression vector (see Example 1). The expression and partial purification of the mutant LacI-derived GST-GR LBD fusion proteins were performed in the same manner as described in Examples 3 and 4.

Figure 1D depicts the partial purification of *E. Coli* expressed GR (521-777) for several mutants isolated by the LacI Fusion system. For solubility testing, these mutants are expressed as a fusion to 6xHis-GST using the modified pET24 expression vector. Continuing with Figure 1D, Lane 1 contains the soluble fraction of GST-GR (521-777) F602S, Lane 2: GR (521-777) wild type, Lane 3: GST-GR (521-777) A580T/F602L, Lane 4: GST-GR (521-777) A574T, Lane 5: GST-GR (521-777) Q615H, and Lane 6: GST-GR (521-777) Q615L. Molecular weight markers (kD) are shown in Lane M.

Table 3
Statistics of Crystallographic Data and Structure

Crystals	GR/TIF2 with dexamethasone
Space group	P6 ₁
resolution (Å)	20.0- 2.8
Unique reflections (N)	18,923
completeness (%)	99.7
I/σ (last shell)	25.6 (2.2)
R _{sym} ^a (%)	8.5
refinement statistics	
R factor ^b (%)	33.4
R free (%)	29.6
r.m.s.d.	
bond lengths (Å)	0.015
r.m.s.d. bond	
angles(degrees)	1.795
Number of H2O	53
total non-hydrogen	4444
atoms	

r.m.s.d is the root mean square deviation from ideal

5 geometry.

$$^aR_{\text{sym}} = \sum |I_{\text{avg}} - I| / \sum I$$

^bR_{factor} = $\sum |F_p - F_{\text{Pcalc}}| / \sum F_p$, where F_p and F_{pcalc} are observed and calculated structure factors, R_{free} is calculated from a randomly chosen 8% of reflections

10 that never be used in refinement and R_{factor} is calculated for the remaining 92% of reflections.

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TABLE 4
 ATOMIC STRUCTURE COORDINATE DATA OBTAINED FROM X-RAY
 DIFFRACTION FROM THE LIGAND BINDING DOMAIN OF GR α IN COMPLEX
 WITH DEXAMETHASONE

5

ATOM	ATOM TYPE	RESIDUE	PROTEIN #	#	X	Y	OCC	B
1	CB	GLN	527	60.207	9.806	35.497	1.00	60.77
2	CG	GLN	527	60.501	11.318	35.564	1.00	60.74
3	CD	GLN	527	60.595	11.993	34.172	1.00	63.52
4	OE1	GLN	527	60.493	13.224	34.058	1.00	61.80
5	NE2	GLN	527	60.794	11.187	33.121	1.00	61.21
6	C	GLN	527	62.073	8.590	36.647	1.00	62.83
7	O	GLN	527	63.240	8.191	36.724	1.00	59.67
8	N	GLN	527	61.009	7.618	34.618	1.00	58.91
9	CA	GLN	527	61.426	8.890	35.289	1.00	62.13
10	N	LEU	528	61.308	8.776	37.716	1.00	62.73
11	CA	LEU	528	61.816	8.538	39.064	1.00	65.02
12	CB	LEU	528	62.105	9.889	39.733	1.00	62.65
13	CG	LEU	528	62.864	10.872	38.813	1.00	59.23
14	CD1	LEU	528	62.071	12.198	38.675	1.00	63.52
15	CD2	LEU	528	64.283	11.105	39.356	1.00	60.04
16	C	LEU	528	60.823	7.690	39.888	1.00	59.38
17	O	LEU	528	60.586	6.527	39.527	1.00	63.35
18	N	THR	529	60.247	8.256	40.960	1.00	60.40
19	CA	THR	529	59.282	7.539	41.835	1.00	60.79
20	CB	THR	529	57.841	8.227	41.847	1.00	63.67
21	OG1	THR	529	57.918	9.561	42.382	1.00	60.60
22	CG2	THR	529	56.867	7.410	42.706	1.00	62.04
23	C	THR	529	59.134	6.056	41.397	1.00	61.38
24	O	THR	529	58.454	5.754	40.398	1.00	59.93
25	N	PRO	530	59.743	5.117	42.163	1.00	61.16
26	CD	PRO	530	60.110	5.411	43.563	1.00	60.38
27	CA	PRO	530	59.753	3.660	41.928	1.00	62.39
28	CB	PRO	530	60.388	3.109	43.213	1.00	58.06
29	CG	PRO	530	59.914	4.071	44.249	1.00	64.31
30	C	PRO	530	58.453	2.927	41.537	1.00	63.39
31	O	PRO	530	57.400	3.542	41.363	1.00	59.17
32	N	THR	531	58.554	1.603	41.419	1.00	62.27
33	CA	THR	531	57.455	0.742	40.997	1.00	61.68
34	CB	THR	531	57.989	-0.404	40.058	1.00	60.38
35	OG1	THR	531	57.209	-0.461	38.853	1.00	60.25
36	CG2	THR	531	57.937	-1.760	40.757	1.00	60.67
37	C	THR	531	56.629	0.125	42.117	1.00	60.82

38	O	THR	531	55.533	-0.361	41.864	1.00	62.20
39	N	LEU	532	57.122	0.128	43.348	1.00	60.85
40	CA	LEU	532	56.324	-0.465	44.418	1.00	60.11
41	CB	LEU	532	57.183	-0.775	45.637	1.00	64.22
42	CG	LEU	532	56.388	-1.514	46.704	1.00	63.74
43	CD1	LEU	532	55.677	-2.694	46.082	1.00	62.66
44	CD2	LEU	532	57.317	-1.968	47.806	1.00	63.22
45	C	LEU	532	55.143	0.422	44.817	1.00	62.08
46	O	LEU	532	54.047	-0.075	45.061	1.00	61.27
47	N	VAL	533	55.366	1.733	44.883	1.00	59.27
48	CA	VAL	533	54.297	2.677	45.222	1.00	62.90
49	CB	VAL	533	54.858	4.050	45.638	1.00	64.91
50	CG1	VAL	533	55.572	4.693	44.465	1.00	60.86
51	CG2	VAL	533	53.746	4.941	46.102	1.00	61.00
52	C	VAL	533	53.422	2.874	43.979	1.00	62.21
53	O	VAL	533	52.281	3.321	44.065	1.00	61.72
54	N	SER	534	53.981	2.553	42.817	1.00	60.92
55	CA	SER	534	53.249	2.665	41.564	1.00	61.24
56	CB	SER	534	54.196	2.474	40.386	1.00	61.92
57	OG	SER	534	53.468	2.355	39.183	1.00	61.38
58	C	SER	534	52.209	1.557	41.566	1.00	64.31
59	O	SER	534	51.105	1.691	41.027	1.00	62.62
60	N	LEU	535	52.581	0.452	42.193	1.00	61.91
61	CA	LEU	535	51.697	-0.684	42.288	1.00	60.97
62	CB	LEU	535	52.479	-1.922	42.730	1.00	66.65
63	CG	LEU	535	51.949	-3.225	42.131	1.00	63.58
64	CD1	LEU	535	52.657	-3.505	40.827	1.00	62.14
65	CD2	LEU	535	52.175	-4.364	43.090	1.00	61.95
66	C	LEU	535	50.588	-0.353	43.285	1.00	59.91
67	O	LEU	535	49.432	-0.684	43.060	1.00	63.02
68	N	LEU	536	50.933	0.315	44.381	1.00	62.58
69	CA	LEU	536	49.932	0.683	45.376	1.00	59.17
70	CB	LEU	536	50.583	1.413	46.541	1.00	61.74
71	CG	LEU	536	51.501	0.625	47.460	1.00	58.87
72	CD1	LEU	536	51.953	1.545	48.553	1.00	59.54
73	CD2	LEU	536	50.781	-0.575	48.045	1.00	63.64
74	C	LEU	536	48.821	1.569	44.812	1.00	63.31
75	O	LEU	536	47.672	1.489	45.256	1.00	61.67
76	N	GLU	537	49.171	2.415	43.845	1.00	59.21
77	CA	GLU	537	48.231	3.343	43.213	1.00	59.76
78	CB	GLU	537	48.984	4.292	42.302	1.00	59.81
79	CG	GLU	537	48.816	5.744	42.625	1.00	60.10
80	CD	GLU	537	48.907	6.616	41.385	1.00	64.34
81	OE1	GLU	537	47.868	6.813	40.707	1.00	57.41
82	OE2	GLU	537	50.024	7.091	41.084	1.00	62.84
83	C	GLU	537	47.139	2.698	42.371	1.00	61.66
84	O	GLU	537	45.973	3.101	42.433	1.00	60.28
85	N	VAL	538	47.536	1.717	41.564	1.00	60.48

86	CA	VAL	538	46.606	1.045	40.674	1.00	63.41
87	CB	VAL	538	47.325	0.448	39.442	1.00	64.15
88	CG1	VAL	538	48.334	1.444	38.903	1.00	60.29
89	CG2	VAL	538	47.973	-0.883	39.797	1.00	63.88
90	C	VAL	538	45.768	-0.046	41.311	1.00	57.99
91	O	VAL	538	44.828	-0.530	40.683	1.00	58.71
92	N	ILE	539	46.094	-0.454	42.535	1.00	61.14
93	CA	ILE	539	45.282	-1.484	43.186	1.00	60.23
94	CB	ILE	539	46.141	-2.499	44.010	1.00	65.32
95	CG2	ILE	539	47.243	-3.066	43.140	1.00	61.32
96	CG1	ILE	539	46.775	-1.833	45.228	1.00	63.80
97	CD1	ILE	539	47.356	-2.833	46.207	1.00	60.85
98	C	ILE	539	44.259	-0.811	44.097	1.00	61.40
99	O	ILE	539	43.321	-1.447	44.573	1.00	63.49
100	N	GLU	540	44.451	0.489	44.310	1.00	61.12
101	CA	GLU	540	43.584	1.307	45.153	1.00	60.76
102	CB	GLU	540	44.109	2.753	45.173	1.00	58.26
103	CG	GLU	540	43.466	3.684	46.191	1.00	61.15
104	CD	GLU	540	43.598	3.183	47.619	1.00	61.95
105	OE1	GLU	540	44.656	2.591	47.950	1.00	59.71
106	OE2	GLU	540	42.649	3.397	48.410	1.00	62.96
107	C	GLU	540	42.169	1.264	44.585	1.00	61.78
108	O	GLU	540	41.928	1.709	43.459	1.00	61.36
109	N	PRO	541	41.214	0.713	45.352	1.00	63.77
110	CD	PRO	541	41.365	0.053	46.659	1.00	58.98
111	CA	PRO	541	39.830	0.632	44.876	1.00	60.14
112	CB	PRO	541	39.131	-0.149	45.988	1.00	59.62
113	CG	PRO	541	39.978	0.122	47.195	1.00	60.56
114	C	PRO	541	39.180	1.991	44.592	1.00	62.36
115	O	PRO	541	39.455	2.982	45.283	1.00	59.45
116	N	GLU	542	38.332	2.039	43.563	1.00	60.43
117	CA	GLU	542	37.653	3.279	43.198	1.00	62.04
118	CB	GLU	542	37.091	3.201	41.770	1.00	62.84
119	CG	GLU	542	36.130	2.050	41.511	1.00	63.24
120	CD	GLU	542	35.745	1.911	40.031	1.00	63.39
121	OE1	GLU	542	36.622	2.095	39.153	1.00	60.50
122	OE2	GLU	542	34.568	1.599	39.743	1.00	59.31
123	C	GLU	542	36.548	3.515	44.208	1.00	63.11
124	O	GLU	542	35.941	2.564	44.697	1.00	59.70
125	N	VAL	543	36.304	4.783	44.528	1.00	61.53
126	CA	VAL	543	35.299	5.148	45.518	1.00	63.47
127	CB	VAL	543	35.334	6.661	45.801	1.00	62.60
128	CG1	VAL	543	34.467	6.984	46.987	1.00	60.93
129	CG2	VAL	543	36.762	7.103	46.064	1.00	59.59
130	C	VAL	543	33.886	4.748	45.126	1.00	61.39
131	O	VAL	543	33.495	4.877	43.965	1.00	60.79
132	N	LEU	544	33.128	4.267	46.109	1.00	62.56
133	CA	LEU	544	31.759	3.836	45.882	1.00	60.63

134	CB	LEU	544	31.501	2.486	46.547	1.00	63.18
135	CG	LEU	544	32.666	1.512	46.682	1.00	61.92
136	CD1	LEU	544	33.702	2.114	47.638	1.00	62.67
137	CD2	LEU	544	32.163	0.172	47.225	1.00	61.02
138	C	LEU	544	30.754	4.844	46.423	1.00	58.48
139	O	LEU	544	31.097	5.715	47.225	1.00	59.01
140	N	TYR	545	29.508	4.698	45.974	1.00	60.35
141	CA	TYR	545	28.394	5.559	46.356	1.00	58.86
142	CB	TYR	545	27.616	5.977	45.105	1.00	59.62
143	CG	TYR	545	28.421	6.799	44.122	1.00	60.54
144	CD1	TYR	545	29.815	6.803	44.162	1.00	59.00
145	CE1	TYR	545	30.561	7.563	43.270	1.00	61.22
146	CD2	TYR	545	27.791	7.579	43.153	1.00	63.95
147	CE2	TYR	545	28.534	8.348	42.256	1.00	59.17
148	CZ	TYR	545	29.914	8.336	42.325	1.00	60.43
149	OH	TYR	545	30.654	9.120	41.478	1.00	60.96
150	C	TYR	545	27.501	4.743	47.269	1.00	64.48
151	O	TYR	545	27.449	3.517	47.151	1.00	60.43
152	N	ALA	546	26.789	5.415	48.168	1.00	62.22
153	CA	ALA	546	25.918	4.720	49.112	1.00	61.72
154	CB	ALA	546	25.780	5.540	50.378	1.00	60.83
155	C	ALA	546	24.536	4.377	48.570	1.00	61.54
156	O	ALA	546	23.886	3.461	49.065	1.00	58.65
157	N	GLY	547	24.089	5.100	47.549	1.00	60.89
158	CA	GLY	547	22.768	4.841	47.014	1.00	59.44
159	C	GLY	547	21.765	5.212	48.088	1.00	59.45
160	O	GLY	547	20.849	4.460	48.392	1.00	58.64
161	N	TYR	548	21.966	6.387	48.671	1.00	59.64
162	CA	TYR	548	21.119	6.921	49.733	1.00	61.47
163	CB	TYR	548	21.912	7.970	50.520	1.00	64.12
164	CG	TYR	548	21.244	8.421	51.783	1.00	58.90
165	CD1	TYR	548	21.049	7.534	52.833	1.00	61.61
166	CE1	TYR	548	20.414	7.927	53.992	1.00	63.67
167	CD2	TYR	548	20.785	9.726	51.926	1.00	60.05
168	CE2	TYR	548	20.144	10.129	53.084	1.00	60.57
169	CZ	TYR	548	19.964	9.218	54.112	1.00	64.94
170	OH	TYR	548	19.319	9.579	55.262	1.00	63.47
171	C	TYR	548	19.907	7.569	49.080	1.00	63.87
172	O	TYR	548	19.755	7.481	47.867	1.00	60.53
173	N	ASP	549	19.043	8.207	49.871	1.00	60.86
174	CA	ASP	549	17.881	8.882	49.307	1.00	62.83
175	CB	ASP	549	16.590	8.410	49.958	1.00	61.82
176	CG	ASP	549	15.487	8.213	48.935	1.00	59.25
177	OD1	ASP	549	14.321	7.942	49.306	1.00	61.06
178	OD2	ASP	549	15.810	8.328	47.734	1.00	61.75
179	C	ASP	549	17.979	10.402	49.411	1.00	62.83
180	O	ASP	549	18.158	11.075	48.400	1.00	60.57
181	N	SER	550	17.875	10.954	50.617	1.00	59.81

182	CA	SER	550	17.953	12.415	50.793	1.00	62.38
183	CB	SER	550	19.325	12.951	50.386	1.00	56.99
184	OG	SER	550	19.438	13.020	48.978	1.00	62.06
185	C	SER	550	16.894	13.126	49.957	1.00	62.44
186	O	SER	550	16.893	14.350	49.843	1.00	61.89
187	N	SER	551	16.018	12.343	49.343	1.00	61.48
188	CA	SER	551	14.924	12.875	48.557	1.00	60.05
189	CB	SER	551	14.507	11.886	47.487	1.00	62.39
190	OG	SER	551	13.838	10.800	48.100	1.00	61.65
191	C	SER	551	13.850	12.904	49.615	1.00	60.87
192	O	SER	551	12.799	13.512	49.452	1.00	59.31
193	N	VAL	552	14.142	12.200	50.703	1.00	61.91
194	CA	VAL	552	13.252	12.096	51.849	1.00	60.13
195	CB	VAL	552	12.584	10.695	51.895	1.00	60.55
196	CG1	VAL	552	11.242	10.744	51.187	1.00	59.77
197	CG2	VAL	552	13.461	9.674	51.211	1.00	62.73
198	C	VAL	552	14.035	12.388	53.141	1.00	58.44
199	O	VAL	552	15.269	12.482	53.116	1.00	60.59
200	N	PRO	553	13.326	12.571	54.278	1.00	59.91
201	CD	PRO	553	11.861	12.614	54.440	1.00	61.19
202	CA	PRO	553	13.974	12.859	55.559	1.00	59.95
203	CB	PRO	553	12.865	12.572	56.556	1.00	62.02
204	CG	PRO	553	11.701	13.166	55.851	1.00	62.09
205	C	PRO	553	15.263	12.093	55.839	1.00	62.80
206	O	PRO	553	15.525	11.035	55.259	1.00	61.14
207	N	ASP	554	16.058	12.646	56.748	1.00	58.85
208	CA	ASP	554	17.357	12.084	57.104	1.00	60.06
209	CB	ASP	554	18.462	13.098	56.755	1.00	61.56
210	CG	ASP	554	18.836	13.106	55.280	1.00	62.42
211	OD1	ASP	554	17.961	12.964	54.390	1.00	59.77
212	OD2	ASP	554	20.038	13.286	55.014	1.00	59.95
213	C	ASP	554	17.535	11.703	58.575	1.00	56.92
214	O	ASP	554	18.402	12.273	59.229	1.00	61.20
215	N	SER	555	16.767	10.761	59.116	1.00	62.60
216	CA	SER	555	16.970	10.398	60.526	1.00	63.72
217	CB	SER	555	15.998	9.296	60.948	1.00	63.32
218	OG	SER	555	16.267	8.089	60.255	1.00	60.75
219	C	SER	555	18.404	9.905	60.749	1.00	61.32
220	O	SER	555	19.093	9.556	59.794	1.00	59.49
221	N	THR	556	18.855	9.877	62.002	1.00	63.20
222	CA	THR	556	20.211	9.407	62.308	1.00	62.68
223	CB	THR	556	20.554	9.487	63.826	1.00	62.64
224	OG1	THR	556	20.893	10.831	64.183	1.00	62.26
225	CG2	THR	556	21.739	8.582	64.158	1.00	62.40
226	C	THR	556	20.387	7.955	61.902	1.00	62.17
227	O	THR	556	21.196	7.633	61.030	1.00	63.77
228	N	TRP	557	19.624	7.082	62.554	1.00	63.04
229	CA	TRP	557	19.696	5.652	62.294	1.00	60.39

230	CB	TRP	557	18.505	4.923	62.964	1.00	61.26
231	CG	TRP	557	17.324	4.805	62.064	1.00	64.02
232	CD2	TRP	557	17.074	3.747	61.123	1.00	60.71
233	CE2	TRP	557	15.970	4.142	60.332	1.00	58.32
234	CE3	TRP	557	17.684	2.511	60.865	1.00	62.45
235	CD1	TRP	557	16.378	5.760	61.825	1.00	60.50
236	NE1	TRP	557	15.562	5.373	60.780	1.00	59.73
237	CZ2	TRP	557	15.464	3.341	59.296	1.00	61.79
238	CZ3	TRP	557	17.184	1.716	59.836	1.00	62.55
239	CH2	TRP	557	16.084	2.136	59.065	1.00	57.76
240	C	TRP	557	19.731	5.362	60.783	1.00	61.95
241	O	TRP	557	20.479	4.493	60.332	1.00	59.61
242	N	ARG	558	18.946	6.099	60.001	1.00	61.85
243	CA	ARG	558	18.898	5.873	58.555	1.00	64.57
244	CB	ARG	558	17.744	6.651	57.926	1.00	59.03
245	CG	ARG	558	17.303	6.107	56.582	1.00	62.63
246	CD	ARG	558	16.012	6.780	56.133	1.00	59.07
247	NE	ARG	558	16.221	7.958	55.288	1.00	61.76
248	CZ	ARG	558	16.594	7.911	54.011	1.00	63.52
249	NH1	ARG	558	16.805	6.745	53.420	1.00	63.08
250	NH2	ARG	558	16.750	9.031	53.319	1.00	60.97
251	C	ARG	558	20.200	6.222	57.841	1.00	64.20
252	O	ARG	558	20.573	5.566	56.869	1.00	65.47
253	N	ILE	559	20.877	7.266	58.307	1.00	62.87
254	CA	ILE	559	22.156	7.678	57.726	1.00	59.66
255	CB	ILE	559	22.639	9.040	58.329	1.00	62.98
256	CG2	ILE	559	24.101	9.278	57.993	1.00	59.64
257	CG1	ILE	559	21.794	10.196	57.791	1.00	61.72
258	CD1	ILE	559	22.091	10.556	56.351	1.00	60.58
259	C	ILE	559	23.152	6.585	58.119	1.00	62.05
260	O	ILE	559	23.838	5.995	57.274	1.00	61.48
261	N	MET	560	23.188	6.332	59.425	1.00	60.47
262	CA	MET	560	24.056	5.340	60.036	1.00	59.72
263	CB	MET	560	23.799	5.286	61.554	1.00	61.50
264	CG	MET	560	24.863	6.016	62.358	1.00	59.68
265	SD	MET	560	24.765	5.946	64.183	1.00	62.00
266	CE	MET	560	25.827	7.029	64.314	1.00	56.75
267	C	MET	560	23.910	3.950	59.421	1.00	63.13
268	O	MET	560	24.908	3.299	59.122	1.00	60.43
269	N	THR	561	22.680	3.493	59.215	1.00	59.86
270	CA	THR	561	22.487	2.183	58.619	1.00	62.03
271	CB	THR	561	21.005	1.771	58.603	1.00	60.73
272	OG1	THR	561	20.483	1.777	59.938	1.00	58.44
273	CG2	THR	561	20.862	0.370	58.025	1.00	59.27
274	C	THR	561	23.005	2.192	57.190	1.00	62.25
275	O	THR	561	23.565	1.211	56.724	1.00	59.53
276	N	THR	562	22.813	3.296	56.482	1.00	61.35
277	CA	THR	562	23.305	3.365	55.112	1.00	62.18

278	CB	THR	562	22.728	4.593	54.342	1.00	58.86
279	OG1	THR	562	21.338	4.375	54.051	1.00	58.36
280	CG2	THR	562	23.473	4.805	53.033	1.00	58.66
281	C	THR	562	24.830	3.432	55.157	1.00	62.40
282	O	THR	562	25.509	3.011	54.225	1.00	59.62
283	N	LEU	563	25.374	3.949	56.252	1.00	60.06
284	CA	LEU	563	26.825	4.026	56.382	1.00	61.98
285	CB	LEU	563	27.230	5.045	57.451	1.00	59.10
286	CG	LEU	563	27.004	6.519	57.119	1.00	62.03
287	CD1	LEU	563	27.667	7.377	58.180	1.00	59.83
288	CD2	LEU	563	27.574	6.827	55.745	1.00	63.51
289	C	LEU	563	27.406	2.657	56.730	1.00	63.21
290	O	LEU	563	28.592	2.410	56.529	1.00	59.14
291	N	ASN	564	26.567	1.773	57.264	1.00	59.68
292	CA	ASN	564	27.001	0.427	57.606	1.00	62.50
293	CB	ASN	564	26.110	-0.166	58.689	1.00	61.63
294	CG	ASN	564	26.456	0.349	60.058	1.00	62.37
295	OD1	ASN	564	27.625	0.513	60.381	1.00	62.36
296	ND2	ASN	564	25.447	0.590	60.881	1.00	59.03
297	C	ASN	564	26.949	-0.442	56.356	1.00	61.40
298	O	ASN	564	27.823	-1.266	56.121	1.00	61.63
299	N	MET	565	25.923	-0.251	55.543	1.00	62.42
300	CA	MET	565	25.804	-1.022	54.320	1.00	63.45
301	CB	MET	565	24.483	-0.701	53.632	1.00	59.10
302	CG	MET	565	23.266	-0.999	54.488	1.00	62.52
303	SD	MET	565	23.154	-2.742	54.883	1.00	63.35
304	CE	MET	565	22.918	-2.702	56.627	1.00	60.16
305	C	MET	565	26.967	-0.669	53.410	1.00	62.27
306	O	MET	565	27.475	-1.509	52.677	1.00	62.01
307	N	LEU	566	27.382	0.590	53.462	1.00	62.25
308	CA	LEU	566	28.495	1.064	52.656	1.00	60.20
309	CB	LEU	566	28.596	2.594	52.741	1.00	59.50
310	CG	LEU	566	29.801	3.267	52.076	1.00	64.18
311	CD1	LEU	566	29.685	3.195	50.565	1.00	61.46
312	CD2	LEU	566	29.869	4.700	52.516	1.00	62.10
313	C	LEU	566	29.756	0.424	53.218	1.00	62.85
314	O	LEU	566	30.576	-0.116	52.474	1.00	60.20
315	N	GLY	567	29.886	0.477	54.542	1.00	59.45
316	CA	GLY	567	31.040	-0.095	55.207	1.00	59.94
317	C	GLY	567	31.316	-1.516	54.768	1.00	60.71
318	O	GLY	567	32.461	-1.890	54.520	1.00	59.79
319	N	GLY	568	30.261	-2.310	54.667	1.00	61.99
320	CA	GLY	568	30.417	-3.687	54.254	1.00	59.73
321	C	GLY	568	31.050	-3.836	52.888	1.00	60.65
322	O	GLY	568	32.008	-4.590	52.724	1.00	63.15
323	N	ARG	569	30.529	-3.112	51.907	1.00	58.99
324	CA	ARG	569	31.049	-3.208	50.557	1.00	60.81
325	CB	ARG	569	30.109	-2.483	49.600	1.00	60.57

326	CG	ARG	569	28.696	-3.029	49.701	1.00	61.60
327	CD	ARG	569	27.806	-2.602	48.556	1.00	64.73
328	NE	ARG	569	27.561	-1.168	48.564	1.00	61.17
329	CZ	ARG	569	27.939	-0.352	47.590	1.00	60.00
330	NH1	ARG	569	28.577	-0.841	46.532	1.00	60.46
331	NH2	ARG	569	27.681	0.946	47.680	1.00	63.69
332	C	ARG	569	32.462	-2.676	50.447	1.00	61.15
333	O	ARG	569	33.249	-3.137	49.620	1.00	60.59
334	N	GLN	570	32.788	-1.713	51.295	1.00	60.73
335	CA	GLN	570	34.123	-1.132	51.300	1.00	62.31
336	CB	GLN	570	34.143	0.150	52.120	1.00	59.04
337	CG	GLN	570	33.608	1.361	51.417	1.00	62.03
338	CD	GLN	570	33.782	2.606	52.247	1.00	56.35
339	OE1	GLN	570	33.460	3.698	51.801	1.00	62.86
340	NE2	GLN	570	34.295	2.449	53.467	1.00	63.17
341	C	GLN	570	35.144	-2.093	51.882	1.00	61.15
342	O	GLN	570	36.293	-2.134	51.441	1.00	60.50
343	N	VAL	571	34.732	-2.837	52.903	1.00	60.99
344	CA	VAL	571	35.615	-3.792	53.554	1.00	61.91
345	CB	VAL	571	35.054	-4.200	54.930	1.00	58.42
346	CG1	VAL	571	35.822	-5.393	55.485	1.00	61.27
347	CG2	VAL	571	35.160	-3.007	55.891	1.00	60.58
348	C	VAL	571	35.805	-5.007	52.665	1.00	62.66
349	O	VAL	571	36.698	-5.820	52.885	1.00	58.99
350	N	ILE	572	34.958	-5.116	51.652	1.00	63.61
351	CA	ILE	572	35.042	-6.206	50.695	1.00	63.76
352	CB	ILE	572	33.649	-6.539	50.103	1.00	60.98
353	CG2	ILE	572	33.794	-7.443	48.883	1.00	63.63
354	CG1	ILE	572	32.782	-7.192	51.183	1.00	61.03
355	CD1	ILE	572	31.346	-7.366	50.801	1.00	62.17
356	C	ILE	572	35.999	-5.772	49.589	1.00	60.35
357	O	ILE	572	36.733	-6.587	49.042	1.00	62.13
358	N	ALA	573	35.984	-4.481	49.265	1.00	62.76
359	CA	ALA	573	36.879	-3.936	48.251	1.00	58.47
360	CB	ALA	573	36.502	-2.496	47.940	1.00	61.48
361	C	ALA	573	38.271	-3.997	48.872	1.00	61.14
362	O	ALA	573	39.294	-4.088	48.180	1.00	60.46
363	N	ALA	574	38.273	-3.964	50.200	1.00	60.84
364	CA	ALA	574	39.477	-4.008	51.003	1.00	61.42
365	CB	ALA	574	39.098	-3.888	52.465	1.00	60.18
366	C	ALA	574	40.294	-5.282	50.771	1.00	58.96
367	O	ALA	574	41.506	-5.217	50.518	1.00	61.38
368	N	VAL	575	39.631	-6.435	50.861	1.00	59.99
369	CA	VAL	575	40.296	-7.720	50.664	1.00	59.60
370	CB	VAL	575	39.309	-8.898	50.732	1.00	56.06
371	CG1	VAL	575	40.070	-10.197	50.570	1.00	62.55
372	CG2	VAL	575	38.547	-8.880	52.057	1.00	63.34
373	C	VAL	575	41.009	-7.779	49.318	1.00	60.96

374	O	VAL	575	42.222	-7.981	49.264	1.00	62.47
375	N	LYS	576	40.265	-7.584	48.236	1.00	59.97
376	CA	LYS	576	40.851	-7.628	46.901	1.00	62.25
377	CB	LYS	576	39.770	-7.391	45.860	1.00	60.99
378	CG	LYS	576	40.115	-7.866	44.462	1.00	61.35
379	CD	LYS	576	38.905	-7.708	43.568	1.00	63.13
380	CE	LYS	576	37.667	-8.234	44.276	1.00	62.07
381	NZ	LYS	576	36.420	-7.912	43.531	1.00	59.76
382	C	LYS	576	41.957	-6.593	46.742	1.00	63.69
383	O	LYS	576	42.673	-6.573	45.742	1.00	59.32
384	N	TRP	577	42.074	-5.723	47.734	1.00	62.59
385	CA	TRP	577	43.091	-4.694	47.734	1.00	62.15
386	CB	TRP	577	42.556	-3.432	48.424	1.00	60.50
387	CG	TRP	577	43.620	-2.458	48.780	1.00	63.03
388	CD2	TRP	577	44.140	-2.200	50.090	1.00	58.79
389	CE2	TRP	577	45.189	-1.272	49.945	1.00	64.04
390	CE3	TRP	577	43.824	-2.668	51.372	1.00	60.56
391	CD1	TRP	577	44.346	-1.698	47.924	1.00	62.09
392	NE1	TRP	577	45.293	-0.983	48.611	1.00	61.93
393	CZ2	TRP	577	45.930	-0.798	51.032	1.00	61.40
394	CZ3	TRP	577	44.566	-2.197	52.458	1.00	59.59
395	CH2	TRP	577	45.607	-1.271	52.277	1.00	61.92
396	C	TRP	577	44.263	-5.272	48.509	1.00	64.09
397	O	TRP	577	45.403	-5.238	48.055	1.00	61.89
398	N	ALA	578	43.958	-5.824	49.678	1.00	60.10
399	CA	ALA	578	44.974	-6.411	50.541	1.00	61.99
400	CB	ALA	578	44.342	-6.937	51.828	1.00	57.97
401	C	ALA	578	45.704	-7.526	49.828	1.00	61.84
402	O	ALA	578	46.890	-7.718	50.034	1.00	60.47
403	N	LYS	579	44.988	-8.251	48.979	1.00	61.79
404	CA	LYS	579	45.573	-9.354	48.233	1.00	60.65
405	CB	LYS	579	44.472	-10.320	47.784	1.00	62.20
406	CG	LYS	579	43.479	-10.656	48.893	1.00	63.14
407	CD	LYS	579	42.688	-11.944	48.636	1.00	58.27
408	CE	LYS	579	41.775	-11.862	47.419	1.00	58.47
409	NZ	LYS	579	41.093	-13.167	47.129	1.00	62.99
410	C	LYS	579	46.389	-8.895	47.024	1.00	61.02
411	O	LYS	579	47.014	-9.713	46.356	1.00	63.16
412	N	ALA	580	46.383	-7.596	46.738	1.00	61.84
413	CA	ALA	580	47.153	-7.079	45.610	1.00	58.94
414	CB	ALA	580	46.339	-6.062	44.817	1.00	61.14
415	C	ALA	580	48.439	-6.446	46.137	1.00	60.40
416	O	ALA	580	49.378	-6.190	45.374	1.00	60.45
417	N	ILE	581	48.465	-6.197	47.445	1.00	60.82
418	CA	ILE	581	49.631	-5.631	48.111	1.00	60.29
419	CB	ILE	581	49.375	-5.412	49.630	1.00	58.24
420	CG2	ILE	581	50.654	-4.997	50.324	1.00	63.40
421	CG1	ILE	581	48.295	-4.353	49.847	1.00	62.12

422	CD1	ILE	581	47.769	-4.324	51.257	1.00	62.13
423	C	ILE	581	50.690	-6.706	47.965	1.00	62.02
424	O	ILE	581	50.541	-7.805	48.500	1.00	61.29
425	N	PRO	582	51.773	-6.412	47.233	1.00	62.24
426	CD	PRO	582	52.137	-5.123	46.623	1.00	61.16
427	CA	PRO	582	52.837	-7.397	47.041	1.00	64.30
428	CB	PRO	582	53.983	-6.563	46.486	1.00	61.32
429	CG	PRO	582	53.294	-5.515	45.720	1.00	57.84
430	C	PRO	582	53.208	-8.082	48.341	1.00	62.26
431	O	PRO	582	53.291	-7.451	49.390	1.00	61.55
432	N	GLY	583	53.413	-9.386	48.268	1.00	60.04
433	CA	GLY	583	53.788	-10.138	49.447	1.00	63.24
434	C	GLY	583	52.721	-10.313	50.509	1.00	58.28
435	O	GLY	583	52.976	-10.962	51.519	1.00	61.03
436	N	PHE	584	51.527	-9.758	50.320	1.00	59.53
437	CA	PHE	584	50.517	-9.932	51.354	1.00	60.33
438	CB	PHE	584	49.356	-8.960	51.200	1.00	59.83
439	CG	PHE	584	48.314	-9.107	52.276	1.00	62.69
440	CD1	PHE	584	48.583	-8.699	53.576	1.00	65.80
441	CD2	PHE	584	47.075	-9.677	52.000	1.00	59.15
442	CE1	PHE	584	47.636	-8.854	54.586	1.00	63.90
443	CE2	PHE	584	46.123	-9.837	53.000	1.00	62.77
444	CZ	PHE	584	46.405	-9.423	54.296	1.00	62.23
445	C	PHE	584	49.960	-11.336	51.359	1.00	59.87
446	O	PHE	584	49.874	-11.967	52.415	1.00	60.23
447	N	ARG	585	49.584	-11.848	50.193	1.00	61.22
448	CA	ARG	585	49.021	-13.183	50.207	1.00	62.87
449	CB	ARG	585	48.025	-13.405	49.042	1.00	61.05
450	CG	ARG	585	48.486	-13.212	47.602	1.00	62.14
451	CD	ARG	585	47.253	-13.326	46.690	1.00	59.51
452	NE	ARG	585	46.321	-14.325	47.226	1.00	57.83
453	CZ	ARG	585	45.253	-14.826	46.592	1.00	62.40
454	NH1	ARG	585	44.934	-14.430	45.360	1.00	64.51
455	NH2	ARG	585	44.509	-15.752	47.194	1.00	62.15
456	C	ARG	585	50.053	-14.290	50.303	1.00	61.04
457	O	ARG	585	49.781	-15.436	49.962	1.00	59.18
458	N	ASN	586	51.232	-13.935	50.811	1.00	59.32
459	CA	ASN	586	52.319	-14.893	51.021	1.00	62.11
460	CB	ASN	586	53.659	-14.329	50.545	1.00	57.88
461	CG	ASN	586	53.910	-14.596	49.071	1.00	62.73
462	OD1	ASN	586	54.772	-13.964	48.450	1.00	64.87
463	ND2	ASN	586	53.164	-15.551	48.504	1.00	63.32
464	C	ASN	586	52.396	-15.218	52.503	1.00	61.24
465	O	ASN	586	53.093	-16.138	52.916	1.00	62.45
466	N	LEU	587	51.692	-14.446	53.314	1.00	62.98
467	CA	LEU	587	51.677	-14.732	54.735	1.00	63.89
468	CB	LEU	587	51.210	-13.502	55.522	1.00	63.58
469	CG	LEU	587	52.163	-12.299	55.501	1.00	63.59

470	CD1	LEU	587	51.405	-11.009	55.348	1.00	58.78
471	CD2	LEU	587	52.967	-12.280	56.773	1.00	60.86
472	C	LEU	587	50.679	-15.879	54.848	1.00	61.92
473	O	LEU	587	50.000	-16.209	53.865	1.00	61.57
474	N	HIS	588	50.598	-16.497	56.024	1.00	57.84
475	CA	HIS	588	49.676	-17.609	56.235	1.00	62.30
476	CB	HIS	588	49.674	-18.016	57.710	1.00	63.47
477	CG	HIS	588	49.180	-19.411	57.962	1.00	62.99
478	CD2	HIS	588	49.817	-20.502	58.447	1.00	58.47
479	ND1	HIS	588	47.886	-19.808	57.705	1.00	57.63
480	CE1	HIS	588	47.748	-21.083	58.021	1.00	60.07
481	NE2	HIS	588	48.905	-21.527	58.474	1.00	61.65
482	C	HIS	588	48.304	-17.100	55.839	1.00	61.24
483	O	HIS	588	48.137	-15.900	55.641	1.00	58.81
484	N	LEU	589	47.325	-17.990	55.714	1.00	60.37
485	CA	LEU	589	45.990	-17.542	55.346	1.00	63.23
486	CB	LEU	589	45.219	-18.626	54.588	1.00	60.24
487	CG	LEU	589	44.233	-18.127	53.516	1.00	59.80
488	CD1	LEU	589	43.798	-19.286	52.630	1.00	65.35
489	CD2	LEU	589	43.025	-17.486	54.148	1.00	61.31
490	C	LEU	589	45.249	-17.184	56.616	1.00	59.85
491	O	LEU	589	44.150	-16.645	56.563	1.00	59.20
492	N	ASP	590	45.852	-17.469	57.763	1.00	60.93
493	CA	ASP	590	45.200	-17.158	59.027	1.00	61.82
494	CB	ASP	590	45.551	-18.204	60.097	1.00	62.69
495	CG	ASP	590	44.823	-19.529	59.898	1.00	58.29
496	OD1	ASP	590	44.642	-19.955	58.738	1.00	59.06
497	OD2	ASP	590	44.447	-20.159	60.910	1.00	64.34
498	C	ASP	590	45.608	-15.771	59.504	1.00	59.77
499	O	ASP	590	44.915	-15.153	60.314	1.00	60.73
500	N	ASP	591	46.734	-15.278	59.001	1.00	59.62
501	CA	ASP	591	47.211	-13.960	59.401	1.00	61.48
502	CB	ASP	591	48.733	-13.861	59.240	1.00	60.79
503	CG	ASP	591	49.479	-14.900	60.065	1.00	57.79
504	OD1	ASP	591	49.012	-15.239	61.176	1.00	66.77
505	OD2	ASP	591	50.543	-15.366	59.606	1.00	65.51
506	C	ASP	591	46.531	-12.927	58.529	1.00	62.56
507	O	ASP	591	46.255	-11.812	58.967	1.00	59.26
508	N	GLN	592	46.278	-13.323	57.285	1.00	62.10
509	CA	GLN	592	45.613	-12.473	56.316	1.00	61.30
510	CB	GLN	592	45.432	-13.227	54.998	1.00	62.26
511	CG	GLN	592	46.751	-13.456	54.277	1.00	60.59
512	CD	GLN	592	46.595	-14.100	52.909	1.00	59.32
513	OE1	GLN	592	45.597	-13.887	52.213	1.00	62.27
514	NE2	GLN	592	47.600	-14.875	52.505	1.00	62.12
515	C	GLN	592	44.269	-12.097	56.906	1.00	64.75
516	O	GLN	592	43.768	-10.993	56.706	1.00	62.08
517	N	MET	593	43.701	-13.028	57.660	1.00	59.14

518	CA	MET	593	42.413	-12.815	58.302	1.00	61.78
519	CB	MET	593	41.740	-14.162	58.597	1.00	58.91
520	CG	MET	593	41.290	-14.935	57.357	1.00	64.30
521	SD	MET	593	40.510	-16.524	57.776	1.00	58.06
522	CE	MET	593	39.514	-16.029	59.273	1.00	61.88
523	C	MET	593	42.571	-12.014	59.594	1.00	61.38
524	O	MET	593	41.802	-11.089	59.837	1.00	60.42
525	N	THR	594	43.565	-12.361	60.415	1.00	61.83
526	CA	THR	594	43.781	-11.648	61.674	1.00	61.88
527	CB	THR	594	44.924	-12.267	62.518	1.00	57.74
528	OG1	THR	594	45.252	-13.571	62.023	1.00	65.18
529	CG2	THR	594	44.489	-12.393	63.977	1.00	62.23
530	C	THR	594	44.127	-10.194	61.378	1.00	62.61
531	O	THR	594	43.673	-9.279	62.071	1.00	60.17
532	N	LEU	595	44.927	-9.987	60.337	1.00	60.31
533	CA	LEU	595	45.325	-8.647	59.938	1.00	61.48
534	CB	LEU	595	46.372	-8.712	58.826	1.00	62.70
535	CG	LEU	595	47.788	-9.074	59.266	1.00	60.61
536	CD1	LEU	595	48.711	-9.054	58.067	1.00	63.20
537	CD2	LEU	595	48.268	-8.083	60.316	1.00	62.58
538	C	LEU	595	44.128	-7.823	59.475	1.00	63.38
539	O	LEU	595	43.835	-6.779	60.051	1.00	60.70
540	N	LEU	596	43.439	-8.290	58.436	1.00	60.66
541	CA	LEU	596	42.282	-7.571	57.924	1.00	60.47
542	CB	LEU	596	41.703	-8.278	56.699	1.00	60.10
543	CG	LEU	596	42.351	-7.811	55.392	1.00	60.73
544	CD1	LEU	596	42.036	-8.767	54.254	1.00	59.40
545	CD2	LEU	596	41.859	-6.407	55.073	1.00	62.48
546	C	LEU	596	41.223	-7.424	58.989	1.00	58.32
547	O	LEU	596	40.451	-6.480	58.965	1.00	61.48
548	N	GLN	597	41.201	-8.354	59.935	1.00	62.48
549	CA	GLN	597	40.230	-8.327	61.031	1.00	64.28
550	CB	GLN	597	40.128	-9.712	61.685	1.00	59.49
551	CG	GLN	597	38.936	-10.561	61.279	1.00	64.66
552	CD	GLN	597	38.972	-11.940	61.920	1.00	60.50
553	OE1	GLN	597	39.080	-12.078	63.149	1.00	60.07
554	NE2	GLN	597	38.881	-12.975	61.087	1.00	65.01
555	C	GLN	597	40.612	-7.314	62.110	1.00	61.61
556	O	GLN	597	39.780	-6.933	62.932	1.00	61.06
557	N	TYR	598	41.875	-6.896	62.097	1.00	64.61
558	CA	TYR	598	42.418	-5.958	63.075	1.00	60.76
559	CB	TYR	598	43.761	-6.468	63.588	1.00	59.35
560	CG	TYR	598	43.692	-7.564	64.613	1.00	63.67
561	CD1	TYR	598	42.509	-8.257	64.850	1.00	61.84
562	CE1	TYR	598	42.451	-9.262	65.812	1.00	61.13
563	CD2	TYR	598	44.820	-7.906	65.358	1.00	61.13
564	CE2	TYR	598	44.774	-8.915	66.322	1.00	62.04
565	CZ	TYR	598	43.588	-9.583	66.544	1.00	60.04

566	OH	TYR	598	43.536	-10.549	67.519	1.00	62.57
567	C	TYR	598	42.639	-4.553	62.549	1.00	62.24
568	O	TYR	598	43.158	-3.690	63.256	1.00	61.45
569	N	SER	599	42.278	-4.312	61.305	1.00	58.28
570	CA	SER	599	42.491	-2.988	60.774	1.00	62.69
571	CB	SER	599	43.837	-2.949	60.046	1.00	62.55
572	OG	SER	599	44.008	-4.083	59.216	1.00	62.72
573	C	SER	599	41.365	-2.525	59.867	1.00	64.40
574	O	SER	599	41.398	-1.405	59.367	1.00	62.40
575	N	TRP	600	40.358	-3.375	59.677	1.00	59.48
576	CA	TRP	600	39.245	-3.026	58.807	1.00	62.88
577	CB	TRP	600	38.073	-4.031	58.932	1.00	64.17
578	CG	TRP	600	37.282	-3.951	60.198	1.00	62.02
579	CD2	TRP	600	36.105	-3.166	60.420	1.00	58.67
580	CE2	TRP	600	35.754	-3.311	61.781	1.00	61.68
581	CE3	TRP	600	35.314	-2.350	59.603	1.00	62.68
582	CD1	TRP	600	37.583	-4.533	61.395	1.00	58.92
583	NE1	TRP	600	36.672	-4.151	62.355	1.00	64.28
584	CZ2	TRP	600	34.648	-2.666	62.342	1.00	61.17
585	CZ3	TRP	600	34.217	-1.711	60.159	1.00	58.94
586	CH2	TRP	600	33.894	-1.871	61.516	1.00	61.08
587	C	TRP	600	38.789	-1.630	59.169	1.00	62.61
588	O	TRP	600	38.533	-0.805	58.308	1.00	62.45
589	N	MET	601	38.744	-1.344	60.458	1.00	63.90
590	CA	MET	601	38.298	-0.049	60.884	1.00	60.96
591	CB	MET	601	37.968	-0.064	62.351	1.00	60.46
592	CG	MET	601	37.139	1.112	62.702	1.00	61.28
593	SD	MET	601	35.774	1.420	61.631	1.00	59.33
594	CE	MET	601	34.684	1.638	62.889	1.00	64.63
595	C	MET	601	39.225	1.129	60.577	1.00	61.08
596	O	MET	601	38.758	2.167	60.114	1.00	60.27
597	N	SER	602	40.521	0.979	60.854	1.00	61.23
598	CA	SER	602	41.488	2.035	60.581	1.00	59.98
599	CB	SER	602	42.872	1.647	61.083	1.00	60.99
600	OG	SER	602	42.783	1.022	62.350	1.00	66.17
601	C	SER	602	41.536	2.214	59.079	1.00	60.99
602	O	SER	602	41.609	3.327	58.581	1.00	64.11
603	N	LEU	603	41.494	1.108	58.351	1.00	59.44
604	CA	LEU	603	41.522	1.185	56.901	1.00	61.46
605	CB	LEU	603	41.402	-0.212	56.280	1.00	59.31
606	CG	LEU	603	42.646	-1.097	56.346	1.00	61.54
607	CD1	LEU	603	42.415	-2.362	55.549	1.00	63.99
608	CD2	LEU	603	43.828	-0.346	55.787	1.00	63.36
609	C	LEU	603	40.386	2.061	56.408	1.00	60.47
610	O	LEU	603	40.599	3.062	55.731	1.00	63.39
611	N	MET	604	39.173	1.688	56.784	1.00	63.54
612	CA	MET	604	38.000	2.417	56.365	1.00	62.81
613	CB	MET	604	36.770	1.623	56.723	1.00	58.90

614	CG	MET	604	36.632	0.429	55.842	1.00	59.86
615	SD	MET	604	37.633	0.438	54.374	1.00	62.53
616	CE	MET	604	36.663	-0.510	53.559	1.00	60.72
617	C	MET	604	37.898	3.832	56.856	1.00	60.43
618	O	MET	604	37.397	4.695	56.132	1.00	62.37
619	N	ALA	605	38.375	4.076	58.072	1.00	59.95
620	CA	ALA	605	38.357	5.409	58.664	1.00	60.49
621	CB	ALA	605	38.667	5.317	60.132	1.00	59.15
622	C	ALA	605	39.381	6.309	57.985	1.00	61.50
623	O	ALA	605	39.071	7.427	57.583	1.00	59.82
624	N	PHE	606	40.608	5.810	57.870	1.00	63.59
625	CA	PHE	606	41.700	6.554	57.258	1.00	60.15
626	CB	PHE	606	42.981	5.713	57.285	1.00	63.75
627	CG	PHE	606	44.237	6.490	56.999	1.00	64.30
628	CD1	PHE	606	44.723	7.424	57.913	1.00	61.77
629	CD2	PHE	606	44.957	6.265	55.829	1.00	60.74
630	CE1	PHE	606	45.910	8.118	57.665	1.00	64.00
631	CE2	PHE	606	46.145	6.955	55.575	1.00	62.47
632	CZ	PHE	606	46.620	7.879	56.496	1.00	63.95
633	C	PHE	606	41.362	6.933	55.825	1.00	61.96
634	O	PHE	606	41.751	7.991	55.356	1.00	60.07
635	N	ALA	607	40.644	6.063	55.126	1.00	62.00
636	CA	ALA	607	40.264	6.338	53.745	1.00	57.50
637	CB	ALA	607	39.888	5.051	53.039	1.00	59.69
638	C	ALA	607	39.105	7.324	53.684	1.00	64.88
639	O	ALA	607	38.931	8.030	52.703	1.00	59.60
640	N	LEU	608	38.292	7.361	54.723	1.00	59.93
641	CA	LEU	608	37.196	8.307	54.725	1.00	61.70
642	CB	LEU	608	36.222	7.972	55.883	1.00	59.57
643	CG	LEU	608	35.125	8.918	56.402	1.00	62.57
644	CD1	LEU	608	34.229	9.360	55.287	1.00	63.51
645	CD2	LEU	608	34.298	8.246	57.488	1.00	59.98
646	C	LEU	608	37.862	9.662	54.935	1.00	61.71
647	O	LEU	608	37.500	10.645	54.294	1.00	57.56
648	N	GLY	609	38.869	9.692	55.806	1.00	59.60
649	CA	GLY	609	39.583	10.920	56.086	1.00	60.49
650	C	GLY	609	40.232	11.505	54.850	1.00	59.17
651	O	GLY	609	40.189	12.710	54.625	1.00	61.65
652	N	TRP	610	40.835	10.650	54.039	1.00	62.47
653	CA	TRP	610	41.488	11.102	52.823	1.00	61.40
654	CB	TRP	610	42.141	9.917	52.123	1.00	62.68
655	CG	TRP	610	42.744	10.264	50.817	1.00	62.61
656	CD2	TRP	610	43.955	10.991	50.604	1.00	61.10
657	CE2	TRP	610	44.139	11.095	49.209	1.00	62.45
658	CE3	TRP	610	44.906	11.565	51.457	1.00	63.78
659	CD1	TRP	610	42.254	9.965	49.582	1.00	58.08
660	NE1	TRP	610	43.086	10.459	48.608	1.00	62.17
661	CZ2	TRP	610	45.238	11.751	48.646	1.00	60.53

662	CZ3	TRP	610	46.001	12.219	50.896	1.00	62.27
663	CH2	TRP	610	46.156	12.305	49.505	1.00	60.31
664	C	TRP	610	40.517	11.797	51.874	1.00	60.80
665	O	TRP	610	40.797	12.866	51.358	1.00	60.72
666	N	ARG	611	39.368	11.191	51.639	1.00	61.36
667	CA	ARG	611	38.412	11.790	50.738	1.00	58.33
668	CB	ARG	611	37.254	10.817	50.486	1.00	62.33
669	CG	ARG	611	37.684	9.490	49.873	1.00	60.18
670	CD	ARG	611	36.476	8.686	49.426	1.00	59.83
671	NE	ARG	611	35.604	8.333	50.544	1.00	61.17
672	CZ	ARG	611	35.817	7.308	51.366	1.00	59.54
673	NH1	ARG	611	36.875	6.528	51.187	1.00	61.47
674	NH2	ARG	611	34.988	7.072	52.376	1.00	62.25
675	C	ARG	611	37.898	13.128	51.277	1.00	62.93
676	O	ARG	611	37.610	14.051	50.502	1.00	61.13
677	N	SER	612	37.806	13.234	52.603	1.00	60.26
678	CA	SER	612	37.321	14.450	53.263	1.00	63.90
679	CB	SER	612	37.057	14.172	54.736	1.00	62.00
680	OG	SER	612	36.011	13.234	54.875	1.00	59.62
681	C	SER	612	38.263	15.637	53.137	1.00	61.68
682	O	SER	612	37.831	16.776	52.975	1.00	59.32
683	N	TYR	613	39.552	15.352	53.226	1.00	64.48
684	CA	TYR	613	40.600	16.351	53.111	1.00	60.97
685	CB	TYR	613	41.920	15.725	53.587	1.00	56.65
686	CG	TYR	613	43.169	16.122	52.830	1.00	60.73
687	CD1	TYR	613	43.569	17.456	52.746	1.00	64.60
688	CE1	TYR	613	44.737	17.812	52.086	1.00	60.79
689	CD2	TYR	613	43.971	15.153	52.229	1.00	61.29
690	CE2	TYR	613	45.142	15.500	51.564	1.00	63.40
691	CZ	TYR	613	45.522	16.830	51.497	1.00	61.75
692	OH	TYR	613	46.690	17.173	50.854	1.00	62.46
693	C	TYR	613	40.712	16.822	51.667	1.00	62.41
694	O	TYR	613	40.954	17.996	51.395	1.00	61.34
695	N	ARG	614	40.511	15.896	50.745	1.00	61.73
696	CA	ARG	614	40.623	16.190	49.328	1.00	61.64
697	CB	ARG	614	40.835	14.880	48.545	1.00	62.80
698	CG	ARG	614	42.274	14.328	48.621	1.00	58.30
699	CD	ARG	614	42.908	14.348	47.242	1.00	60.57
700	NE	ARG	614	44.369	14.448	47.262	1.00	61.63
701	CZ	ARG	614	45.056	15.421	47.868	1.00	63.66
702	NH1	ARG	614	44.414	16.386	48.521	1.00	61.59
703	NH2	ARG	614	46.389	15.451	47.797	1.00	64.70
704	C	ARG	614	39.440	16.960	48.776	1.00	58.09
705	O	ARG	614	39.613	17.922	48.041	1.00	63.07
706	N	GLN	615	38.239	16.538	49.137	1.00	64.09
707	CA	GLN	615	37.033	17.192	48.660	1.00	61.67
708	CB	GLN	615	35.840	16.259	48.801	1.00	62.84
709	CG	GLN	615	35.738	15.162	47.795	1.00	62.14

710	CD	GLN	615	34.290	14.775	47.573	1.00	58.76
711	OE1	GLN	615	33.532	14.598	48.525	1.00	62.70
712	NE2	GLN	615	33.897	14.651	46.314	1.00	61.03
713	C	GLN	615	36.677	18.478	49.396	1.00	59.82
714	O	GLN	615	36.200	19.441	48.784	1.00	60.64
715	N	SER	616	36.901	18.480	50.709	1.00	62.12
716	CA	SER	616	36.522	19.615	51.545	1.00	62.52
717	CB	SER	616	35.199	19.297	52.239	1.00	61.86
718	OG	SER	616	35.408	18.310	53.240	1.00	59.96
719	C	SER	616	37.514	20.090	52.612	1.00	61.77
720	O	SER	616	37.110	20.501	53.703	1.00	63.13
721	N	SER	617	38.804	20.026	52.321	1.00	59.65
722	CA	SER	617	39.796	20.502	53.279	1.00	60.19
723	CB	SER	617	39.818	22.033	53.253	1.00	60.71
724	OG	SER	617	39.578	22.511	51.942	1.00	63.01
725	C	SER	617	39.569	20.029	54.724	1.00	59.81
726	O	SER	617	40.164	20.577	55.654	1.00	63.66
727	N	ALA	618	38.700	19.036	54.903	1.00	64.87
728	CA	ALA	618	38.393	18.444	56.210	1.00	62.57
729	CB	ALA	618	39.673	18.327	57.064	1.00	60.83
730	C	ALA	618	37.277	19.059	57.053	1.00	59.66
731	O	ALA	618	37.238	18.817	58.260	1.00	60.80
732	N	ASN	619	36.375	19.839	56.451	1.00	63.98
733	CA	ASN	619	35.262	20.411	57.227	1.00	61.08
734	CB	ASN	619	35.129	21.934	57.042	1.00	61.69
735	CG	ASN	619	35.946	22.453	55.912	1.00	62.23
736	OD1	ASN	619	35.664	22.172	54.751	1.00	61.72
737	ND2	ASN	619	36.980	23.217	56.239	1.00	61.09
738	C	ASN	619	33.907	19.755	56.958	1.00	60.70
739	O	ASN	619	32.856	20.374	57.157	1.00	60.32
740	N	LEU	620	33.951	18.505	56.500	1.00	59.87
741	CA	LEU	620	32.767	17.686	56.237	1.00	59.97
742	CB	LEU	620	31.777	18.358	55.270	1.00	59.52
743	CG	LEU	620	32.162	19.088	53.990	1.00	61.28
744	CD1	LEU	620	31.041	18.989	52.971	1.00	64.28
745	CD2	LEU	620	32.459	20.539	54.330	1.00	65.45
746	C	LEU	620	33.147	16.307	55.712	1.00	61.40
747	O	LEU	620	33.869	16.178	54.720	1.00	61.10
748	N	LEU	621	32.660	15.280	56.407	1.00	58.95
749	CA	LEU	621	32.926	13.891	56.050	1.00	61.88
750	CB	LEU	621	32.394	12.947	57.123	1.00	63.38
751	CG	LEU	621	33.031	13.049	58.503	1.00	60.66
752	CD1	LEU	621	32.383	12.036	59.434	1.00	59.80
753	CD2	LEU	621	34.524	12.808	58.390	1.00	62.77
754	C	LEU	621	32.283	13.540	54.728	1.00	62.48
755	O	LEU	621	31.092	13.751	54.531	1.00	61.33
756	N	CYS	622	33.077	12.972	53.833	1.00	59.02
757	CA	CYS	622	32.585	12.609	52.523	1.00	62.42

758	CB	CYS	622	33.453	13.304	51.479	1.00	59.42
759	SG	CYS	622	33.715	15.064	51.889	1.00	59.94
760	C	CYS	622	32.566	11.094	52.329	1.00	59.63
761	O	CYS	622	33.248	10.552	51.451	1.00	58.28
762	N	PHE	623	31.766	10.421	53.156	1.00	62.39
763	CA	PHE	623	31.645	8.972	53.088	1.00	60.88
764	CB	PHE	623	30.387	8.490	53.841	1.00	59.68
765	CG	PHE	623	30.461	8.686	55.344	1.00	58.52
766	CD1	PHE	623	30.338	9.948	55.906	1.00	66.23
767	CD2	PHE	623	30.688	7.612	56.191	1.00	63.42
768	CE1	PHE	623	30.443	10.139	57.292	1.00	60.25
769	CE2	PHE	623	30.795	7.796	57.576	1.00	58.96
770	CZ	PHE	623	30.673	9.059	58.124	1.00	57.60
771	C	PHE	623	31.618	8.532	51.630	1.00	61.75
772	O	PHE	623	32.502	7.802	51.179	1.00	60.41
773	N	ALA	624	30.624	8.995	50.888	1.00	64.49
774	CA	ALA	624	30.517	8.644	49.476	1.00	61.68
775	CB	ALA	624	29.429	7.592	49.276	1.00	60.07
776	C	ALA	624	30.179	9.912	48.700	1.00	60.93
777	O	ALA	624	30.002	10.981	49.297	1.00	60.98
778	N	PRO	625	30.130	9.828	47.355	1.00	62.43
779	CD	PRO	625	30.706	8.811	46.459	1.00	62.52
780	CA	PRO	625	29.795	11.035	46.593	1.00	59.45
781	CB	PRO	625	29.949	10.582	45.146	1.00	62.18
782	CG	PRO	625	31.089	9.653	45.245	1.00	59.91
783	C	PRO	625	28.366	11.397	46.928	1.00	62.94
784	O	PRO	625	28.111	12.382	47.622	1.00	59.36
785	N	ASP	626	27.433	10.572	46.468	1.00	58.86
786	CA	ASP	626	26.036	10.848	46.741	1.00	60.61
787	CB	ASP	626	25.126	9.882	45.939	1.00	65.12
788	CG	ASP	626	25.227	8.421	46.393	1.00	60.28
789	OD1	ASP	626	25.311	8.160	47.612	1.00	60.31
790	OD2	ASP	626	25.189	7.526	45.518	1.00	59.51
791	C	ASP	626	25.680	10.825	48.248	1.00	58.60
792	O	ASP	626	24.510	10.636	48.616	1.00	62.03
793	N	LEU	627	26.668	11.051	49.119	1.00	63.43
794	CA	LEU	627	26.392	11.020	50.552	1.00	61.63
795	CB	LEU	627	26.175	9.573	51.007	1.00	58.45
796	CG	LEU	627	25.874	9.407	52.496	1.00	63.46
797	CD1	LEU	627	24.401	9.669	52.770	1.00	60.41
798	CD2	LEU	627	26.241	8.013	52.919	1.00	65.05
799	C	LEU	627	27.435	11.665	51.459	1.00	61.00
800	O	LEU	627	28.320	10.988	51.985	1.00	62.27
801	N	ILE	628	27.301	12.965	51.682	1.00	59.87
802	CA	ILE	628	28.230	13.686	52.537	1.00	61.72
803	CB	ILE	628	28.796	14.887	51.787	1.00	61.79
804	CG2	ILE	628	29.848	15.575	52.618	1.00	61.82
805	CG1	ILE	628	29.391	14.418	50.461	1.00	58.81

806	CD1	ILE	628	29.806	15.542	49.554	1.00	61.23
807	C	ILE	628	27.541	14.162	53.815	1.00	59.57
808	O	ILE	628	26.396	14.611	53.779	1.00	61.09
809	N	ILE	629	28.221	14.044	54.951	1.00	60.22
810	CA	ILE	629	27.638	14.493	56.208	1.00	60.98
811	CB	ILE	629	28.261	13.766	57.423	1.00	65.92
812	CG2	ILE	629	28.292	14.681	58.647	1.00	62.88
813	CG1	ILE	629	27.419	12.536	57.768	1.00	64.60
814	CD1	ILE	629	26.917	11.766	56.571	1.00	63.67
815	C	ILE	629	27.852	15.989	56.319	1.00	60.46
816	O	ILE	629	28.935	16.452	56.676	1.00	60.38
817	N	ASN	630	26.797	16.729	55.994	1.00	61.49
818	CA	ASN	630	26.789	18.187	56.015	1.00	61.95
819	CB	ASN	630	25.655	18.685	55.149	1.00	60.74
820	CG	ASN	630	24.348	18.042	55.516	1.00	63.39
821	OD1	ASN	630	24.011	17.949	56.688	1.00	62.29
822	ND2	ASN	630	23.603	17.591	54.525	1.00	63.08
823	C	ASN	630	26.616	18.786	57.402	1.00	63.46
824	O	ASN	630	26.311	18.085	58.369	1.00	63.49
825	N	GLU	631	26.794	20.103	57.475	1.00	60.97
826	CA	GLU	631	26.658	20.840	58.729	1.00	59.85
827	CB	GLU	631	26.743	22.349	58.484	1.00	62.90
828	CG	GLU	631	26.784	23.166	59.774	1.00	60.34
829	CD	GLU	631	25.819	24.340	59.761	1.00	60.36
830	OE1	GLU	631	24.688	24.184	60.288	1.00	62.28
831	OE2	GLU	631	26.191	25.406	59.213	1.00	56.78
832	C	GLU	631	25.313	20.519	59.367	1.00	59.95
833	O	GLU	631	25.223	20.250	60.564	1.00	61.19
834	N	GLN	632	24.268	20.540	58.552	1.00	60.53
835	CA	GLN	632	22.933	20.248	59.046	1.00	60.62
836	CB	GLN	632	21.930	20.354	57.895	1.00	64.85
837	CG	GLN	632	22.121	21.610	57.031	1.00	59.39
838	CD	GLN	632	22.081	22.917	57.841	1.00	63.65
839	OE1	GLN	632	21.068	23.248	58.473	1.00	59.92
840	NE2	GLN	632	23.193	23.663	57.821	1.00	62.67
841	C	GLN	632	22.873	18.860	59.697	1.00	63.23
842	O	GLN	632	22.554	18.741	60.882	1.00	61.37
843	N	ARG	633	23.213	17.827	58.929	1.00	62.09
844	CA	ARG	633	23.190	16.444	59.406	1.00	61.43
845	CB	ARG	633	23.762	15.504	58.345	1.00	60.38
846	CG	ARG	633	22.863	15.388	57.142	1.00	58.68
847	CD	ARG	633	23.419	14.459	56.102	1.00	63.71
848	NE	ARG	633	22.589	14.486	54.905	1.00	62.14
849	CZ	ARG	633	22.885	13.852	53.780	1.00	60.28
850	NH1	ARG	633	23.996	13.136	53.704	1.00	60.27
851	NH2	ARG	633	22.075	13.937	52.733	1.00	60.98
852	C	ARG	633	23.833	16.137	60.753	1.00	64.07
853	O	ARG	633	23.495	15.117	61.348	1.00	60.29

854	N	MET	634	24.758	16.970	61.236	1.00	61.53
855	CA	MET	634	25.334	16.721	62.560	1.00	60.63
856	CB	MET	634	26.429	17.747	62.859	1.00	60.06
857	CG	MET	634	27.598	17.688	61.874	1.00	53.30
858	SD	MET	634	28.604	16.178	62.057	1.00	63.04
859	CE	MET	634	30.133	16.562	61.162	1.00	60.95
860	C	MET	634	24.150	16.834	63.555	1.00	60.65
861	O	MET	634	23.899	17.897	64.149	1.00	63.14
862	N	THR	635	23.420	15.714	63.670	1.00	63.54
863	CA	THR	635	22.220	15.523	64.504	1.00	61.73
864	CB	THR	635	21.180	14.557	63.819	1.00	59.70
865	OG1	THR	635	20.987	14.911	62.442	1.00	57.94
866	CG2	THR	635	19.829	14.609	64.552	1.00	63.34
867	C	THR	635	22.593	14.861	65.825	1.00	61.33
868	O	THR	635	23.570	15.251	66.464	1.00	63.49
869	N	LEU	636	21.796	13.851	66.198	1.00	60.18
870	CA	LEU	636	21.953	13.057	67.420	1.00	61.62
871	CB	LEU	636	22.112	11.577	67.095	1.00	60.70
872	CG	LEU	636	22.867	10.855	68.213	1.00	62.64
873	CD1	LEU	636	21.904	10.048	69.070	1.00	63.15
874	CD2	LEU	636	23.910	9.960	67.603	1.00	60.79
875	C	LEU	636	23.183	13.478	68.172	1.00	61.59
876	O	LEU	636	24.287	13.372	67.626	1.00	60.57
877	N	PRO	637	23.029	13.907	69.442	1.00	59.83
878	CD	PRO	637	22.008	13.402	70.379	1.00	57.71
879	CA	PRO	637	24.225	14.321	70.182	1.00	61.11
880	CB	PRO	637	23.810	14.133	71.639	1.00	61.28
881	CG	PRO	637	22.862	12.966	71.555	1.00	61.68
882	C	PRO	637	25.417	13.433	69.793	1.00	61.18
883	O	PRO	637	26.457	13.928	69.331	1.00	61.45
884	N	CYS	638	25.243	12.117	69.920	1.00	63.53
885	CA	CYS	638	26.333	11.211	69.588	1.00	61.78
886	CB	CYS	638	26.024	9.787	70.065	1.00	62.20
887	SG	CYS	638	24.449	9.498	70.917	1.00	60.82
888	C	CYS	638	26.722	11.209	68.101	1.00	61.50
889	O	CYS	638	27.863	10.844	67.765	1.00	61.11
890	N	MET	639	25.816	11.625	67.214	1.00	57.65
891	CA	MET	639	26.186	11.638	65.817	1.00	60.56
892	CB	MET	639	25.103	12.211	64.924	1.00	66.32
893	CG	MET	639	25.612	12.161	63.532	1.00	60.47
894	SD	MET	639	25.084	11.084	62.238	1.00	57.31
895	CE	MET	639	25.984	11.962	61.115	1.00	58.45
896	C	MET	639	27.478	12.449	65.637	1.00	62.26
897	O	MET	639	28.361	12.083	64.857	1.00	61.35
898	N	TYR	640	27.589	13.543	66.383	1.00	61.78
899	CA	TYR	640	28.797	14.339	66.340	1.00	61.48
900	CB	TYR	640	28.569	15.755	66.872	1.00	60.05
901	CG	TYR	640	29.871	16.511	66.956	1.00	61.42

902	CD1	TYR	640	30.530	16.927	65.795	1.00	62.42
903	CE1	TYR	640	31.800	17.472	65.846	1.00	61.93
904	CD2	TYR	640	30.519	16.680	68.175	1.00	59.45
905	CE2	TYR	640	31.785	17.222	68.235	1.00	63.13
906	CZ	TYR	640	32.425	17.612	67.068	1.00	58.88
907	OH	TYR	640	33.711	18.103	67.130	1.00	60.76
908	C	TYR	640	29.842	13.646	67.215	1.00	60.30
909	O	TYR	640	31.041	13.847	67.034	1.00	63.06
910	N	ASP	641	29.397	12.830	68.168	1.00	61.14
911	CA	ASP	641	30.349	12.136	69.035	1.00	62.18
912	CB	ASP	641	29.674	11.669	70.323	1.00	59.68
913	CG	ASP	641	29.145	12.828	71.135	1.00	60.96
914	OD1	ASP	641	27.930	13.090	71.062	1.00	61.07
915	OD2	ASP	641	29.950	13.493	71.824	1.00	63.74
916	C	ASP	641	30.991	10.971	68.313	1.00	60.81
917	O	ASP	641	32.047	10.482	68.721	1.00	60.52
918	N	GLN	642	30.349	10.542	67.229	1.00	59.76
919	CA	GLN	642	30.860	9.456	66.396	1.00	63.97
920	CB	GLN	642	29.721	8.763	65.687	1.00	61.51
921	CG	GLN	642	28.690	8.348	66.642	1.00	61.79
922	CD	GLN	642	27.547	7.724	65.978	1.00	62.69
923	OE1	GLN	642	27.709	6.684	65.308	1.00	61.01
924	NE2	GLN	642	26.355	8.326	66.145	1.00	60.03
925	C	GLN	642	31.766	10.069	65.359	1.00	62.81
926	O	GLN	642	32.954	9.760	65.294	1.00	61.10
927	N	CYS	643	31.190	10.957	64.556	1.00	60.88
928	CA	CYS	643	31.931	11.628	63.504	1.00	61.65
929	CB	CYS	643	30.977	12.508	62.694	1.00	61.95
930	SG	CYS	643	29.662	11.585	61.843	1.00	63.26
931	C	CYS	643	33.081	12.455	64.071	1.00	61.30
932	O	CYS	643	34.102	12.652	63.418	1.00	61.90
933	N	LYS	644	32.911	12.923	65.299	1.00	62.82
934	CA	LYS	644	33.923	13.730	65.951	1.00	58.73
935	CB	LYS	644	33.634	13.827	67.449	1.00	63.83
936	CG	LYS	644	34.630	14.686	68.207	1.00	59.96
937	CD	LYS	644	34.226	14.891	69.665	1.00	59.57
938	CE	LYS	644	35.160	15.902	70.358	1.00	59.22
939	NZ	LYS	644	35.201	17.239	69.668	1.00	61.66
940	C	LYS	644	35.328	13.182	65.747	1.00	61.72
941	O	LYS	644	36.296	13.941	65.673	1.00	61.77
942	N	HIS	645	35.451	11.864	65.655	1.00	61.41
943	CA	HIS	645	36.769	11.262	65.474	1.00	59.96
944	CB	HIS	645	36.856	9.943	66.209	1.00	60.26
945	CG	HIS	645	37.109	10.100	67.667	1.00	59.75
946	CD2	HIS	645	38.254	10.338	68.346	1.00	58.42
947	ND1	HIS	645	36.103	10.041	68.606	1.00	61.77
948	CE1	HIS	645	36.621	10.232	69.805	1.00	58.75
949	NE2	HIS	645	37.924	10.415	69.675	1.00	57.48

950	C	HIS	645	37.165	11.038	64.037	1.00	60.84
951	O	HIS	645	38.352	11.000	63.727	1.00	62.12
952	N	MET	646	36.172	10.856	63.174	1.00	63.11
953	CA	MET	646	36.432	10.651	61.759	1.00	62.74
954	CB	MET	646	35.135	10.211	61.023	1.00	61.50
955	CG	MET	646	34.686	8.771	61.338	1.00	58.88
956	SD	MET	646	32.994	8.315	60.876	1.00	61.92
957	CE	MET	646	32.426	8.134	62.441	1.00	62.24
958	C	MET	646	36.948	11.972	61.168	1.00	63.61
959	O	MET	646	37.709	11.962	60.197	1.00	63.12
960	N	LEU	647	36.543	13.093	61.772	1.00	60.39
961	CA	LEU	647	36.963	14.419	61.325	1.00	61.16
962	CB	LEU	647	36.105	15.510	61.965	1.00	62.09
963	CG	LEU	647	34.661	15.778	61.551	1.00	62.69
964	CD1	LEU	647	34.144	16.850	62.479	1.00	59.66
965	CD2	LEU	647	34.553	16.232	60.098	1.00	61.60
966	C	LEU	647	38.400	14.652	61.731	1.00	62.99
967	O	LEU	647	39.164	15.329	61.042	1.00	62.41
968	N	TYR	648	38.750	14.087	62.876	1.00	60.24
969	CA	TYR	648	40.087	14.202	63.431	1.00	60.92
970	CB	TYR	648	40.190	13.339	64.685	1.00	59.63
971	CG	TYR	648	41.486	13.510	65.428	1.00	60.33
972	CD1	TYR	648	42.672	12.950	64.952	1.00	62.96
973	CE1	TYR	648	43.876	13.160	65.609	1.00	61.51
974	CD2	TYR	648	41.537	14.280	66.585	1.00	57.67
975	CE2	TYR	648	42.735	14.500	67.252	1.00	62.62
976	CZ	TYR	648	43.902	13.938	66.759	1.00	60.16
977	OH	TYR	648	45.089	14.157	67.426	1.00	64.40
978	C	TYR	648	41.164	13.787	62.435	1.00	61.32
979	O	TYR	648	42.045	14.575	62.099	1.00	62.83
980	N	VAL	649	41.107	12.545	61.971	1.00	65.90
981	CA	VAL	649	42.105	12.079	61.027	1.00	60.14
982	CB	VAL	649	41.862	10.578	60.642	1.00	59.02
983	CG1	VAL	649	40.528	10.109	61.218	1.00	60.92
984	CG2	VAL	649	41.930	10.372	59.122	1.00	59.70
985	C	VAL	649	42.072	12.982	59.814	1.00	61.99
986	O	VAL	649	43.105	13.378	59.297	1.00	60.55
987	N	SER	650	40.873	13.339	59.390	1.00	61.60
988	CA	SER	650	40.705	14.191	58.226	1.00	61.66
989	CB	SER	650	39.224	14.356	57.914	1.00	61.34
990	OG	SER	650	39.069	14.979	56.662	1.00	64.56
991	C	SER	650	41.344	15.555	58.429	1.00	61.44
992	O	SER	650	41.800	16.181	57.476	1.00	58.88
993	N	SER	651	41.365	16.013	59.677	1.00	59.26
994	CA	SER	651	41.960	17.298	60.029	1.00	62.47
995	CB	SER	651	41.578	17.637	61.483	1.00	58.62
996	OG	SER	651	42.537	18.441	62.154	1.00	60.41
997	C	SER	651	43.480	17.204	59.849	1.00	61.76

998	O	SER	651	44.087	18.019	59.164	1.00	62.09
999	N	GLU	652	44.070	16.172	60.441	1.00	60.41
1000	CA	GLU	652	45.509	15.927	60.395	1.00	60.48
1001	CB	GLU	652	45.837	14.680	61.220	1.00	65.10
1002	CG	GLU	652	45.488	14.822	62.677	1.00	59.36
1003	CD	GLU	652	46.160	16.021	63.289	1.00	62.29
1004	OE1	GLU	652	47.399	15.970	63.444	1.00	60.10
1005	OE2	GLU	652	45.451	17.014	63.592	1.00	60.61
1006	C	GLU	652	46.100	15.773	59.001	1.00	59.16
1007	O	GLU	652	47.238	16.166	58.755	1.00	59.92
1008	N	LEU	653	45.335	15.180	58.094	1.00	60.01
1009	CA	LEU	653	45.807	14.984	56.731	1.00	61.61
1010	CB	LEU	653	44.874	14.048	55.960	1.00	64.78
1011	CG	LEU	653	44.860	12.600	56.432	1.00	63.03
1012	CD1	LEU	653	43.723	11.868	55.768	1.00	60.96
1013	CD2	LEU	653	46.179	11.941	56.122	1.00	62.70
1014	C	LEU	653	45.878	16.328	56.037	1.00	60.72
1015	O	LEU	653	46.805	16.588	55.269	1.00	61.12
1016	N	HIS	654	44.895	17.182	56.303	1.00	62.78
1017	CA	HIS	654	44.894	18.497	55.698	1.00	61.32
1018	CB	HIS	654	43.513	19.141	55.805	1.00	63.28
1019	CG	HIS	654	43.517	20.607	55.518	1.00	61.88
1020	CD2	HIS	654	43.210	21.296	54.394	1.00	59.76
1021	ND1	HIS	654	43.946	21.543	56.436	1.00	58.15
1022	CE1	HIS	654	43.905	22.744	55.889	1.00	62.74
1023	NE2	HIS	654	43.463	22.622	54.650	1.00	60.79
1024	C	HIS	654	45.935	19.319	56.440	1.00	62.39
1025	O	HIS	654	46.667	20.112	55.851	1.00	62.10
1026	N	ARG	655	46.012	19.098	57.743	1.00	62.07
1027	CA	ARG	655	46.968	19.804	58.572	1.00	62.85
1028	CB	ARG	655	46.882	19.277	60.008	1.00	58.45
1029	CG	ARG	655	47.082	20.314	61.111	1.00	57.53
1030	CD	ARG	655	48.522	20.368	61.565	1.00	58.48
1031	NE	ARG	655	48.968	19.079	62.082	1.00	61.43
1032	CZ	ARG	655	50.206	18.831	62.503	1.00	59.99
1033	NH1	ARG	655	51.125	19.790	62.472	1.00	61.84
1034	NH2	ARG	655	50.537	17.625	62.950	1.00	60.75
1035	C	ARG	655	48.367	19.599	57.999	1.00	60.66
1036	O	ARG	655	49.086	20.566	57.753	1.00	62.69
1037	N	LEU	656	48.735	18.340	57.759	1.00	60.05
1038	CA	LEU	656	50.060	18.008	57.224	1.00	61.69
1039	CB	LEU	656	50.575	16.697	57.832	1.00	60.63
1040	CG	LEU	656	50.902	16.651	59.330	1.00	60.12
1041	CD1	LEU	656	51.059	15.205	59.759	1.00	61.83
1042	CD2	LEU	656	52.161	17.440	59.632	1.00	61.33
1043	C	LEU	656	50.164	17.922	55.706	1.00	60.82
1044	O	LEU	656	51.187	17.491	55.184	1.00	63.77
1045	N	GLN	657	49.119	18.321	54.995	1.00	62.25

1046	CA	GLN	657	49.165	18.291	53.543	1.00	62.13
1047	CB	GLN	657	50.018	19.442	53.026	1.00	59.95
1048	CG	GLN	657	49.412	20.805	53.219	1.00	60.54
1049	CD	GLN	657	48.109	20.944	52.480	1.00	59.94
1050	OE1	GLN	657	47.043	20.616	52.997	1.00	61.59
1051	NE2	GLN	657	48.189	21.413	51.250	1.00	59.69
1052	C	GLN	657	49.756	16.998	53.027	1.00	64.37
1053	O	GLN	657	50.684	17.013	52.230	1.00	60.80
1054	N	VAL	658	49.233	15.876	53.487	1.00	59.26
1055	CA	VAL	658	49.730	14.589	53.048	1.00	60.79
1056	CB	VAL	658	49.044	13.466	53.856	1.00	61.35
1057	CG1	VAL	658	49.169	12.130	53.154	1.00	61.79
1058	CG2	VAL	658	49.663	13.406	55.240	1.00	61.37
1059	C	VAL	658	49.494	14.416	51.552	1.00	60.15
1060	O	VAL	658	48.452	14.798	51.025	1.00	60.95
1061	N	SER	659	50.485	13.862	50.869	1.00	63.41
1062	CA	SER	659	50.399	13.615	49.438	1.00	58.10
1063	CB	SER	659	51.797	13.685	48.834	1.00	59.86
1064	OG	SER	659	52.018	12.643	47.905	1.00	62.03
1065	C	SER	659	49.777	12.242	49.157	1.00	62.11
1066	O	SER	659	49.781	11.353	50.015	1.00	61.38
1067	N	TYR	660	49.243	12.062	47.956	1.00	60.30
1068	CA	TYR	660	48.633	10.789	47.601	1.00	61.68
1069	CB	TYR	660	48.100	10.860	46.177	1.00	61.85
1070	CG	TYR	660	47.411	9.605	45.727	1.00	59.67
1071	CD1	TYR	660	46.561	8.911	46.581	1.00	63.51
1072	CE1	TYR	660	45.893	7.783	46.152	1.00	60.60
1073	CD2	TYR	660	47.576	9.134	44.431	1.00	60.37
1074	CE2	TYR	660	46.911	8.011	43.990	1.00	64.13
1075	CZ	TYR	660	46.072	7.339	44.851	1.00	63.85
1076	OH	TYR	660	45.393	6.229	44.402	1.00	62.07
1077	C	TYR	660	49.584	9.594	47.749	1.00	59.81
1078	O	TYR	660	49.175	8.510	48.165	1.00	64.86
1079	N	GLU	661	50.853	9.789	47.411	1.00	60.25
1080	CA	GLU	661	51.814	8.703	47.527	1.00	62.48
1081	CB	GLU	661	53.119	9.034	46.788	1.00	61.23
1082	CG	GLU	661	53.209	8.405	45.395	1.00	63.67
1083	CD	GLU	661	54.517	8.708	44.672	1.00	65.78
1084	OE1	GLU	661	55.602	8.472	45.247	1.00	60.21
1085	OE2	GLU	661	54.462	9.174	43.517	1.00	60.28
1086	C	GLU	661	52.096	8.354	48.980	1.00	61.69
1087	O	GLU	661	52.247	7.183	49.312	1.00	61.32
1088	N	GLU	662	52.160	9.348	49.854	1.00	62.68
1089	CA	GLU	662	52.405	9.048	51.252	1.00	63.61
1090	CB	GLU	662	52.605	10.340	52.032	1.00	61.04
1091	CG	GLU	662	53.485	11.321	51.309	1.00	61.12
1092	CD	GLU	662	53.768	12.555	52.117	1.00	62.85
1093	OE1	GLU	662	52.822	13.164	52.637	1.00	58.86

1094	OE2	GLU	662	54.945	12.931	52.227	1.00	61.02
1095	C	GLU	662	51.193	8.277	51.784	1.00	59.86
1096	O	GLU	662	51.333	7.263	52.466	1.00	63.08
1097	N	TYR	663	50.007	8.771	51.436	1.00	61.62
1098	CA	TYR	663	48.716	8.186	51.812	1.00	62.54
1099	CB	TYR	663	47.601	8.921	51.068	1.00	63.89
1100	CG	TYR	663	46.266	8.230	51.167	1.00	61.84
1101	CD1	TYR	663	45.619	8.109	52.392	1.00	59.60
1102	CE1	TYR	663	44.407	7.458	52.498	1.00	58.52
1103	CD2	TYR	663	45.659	7.676	50.043	1.00	58.65
1104	CE2	TYR	663	44.441	7.019	50.138	1.00	60.83
1105	CZ	TYR	663	43.820	6.916	51.368	1.00	62.58
1106	OH	TYR	663	42.601	6.287	51.477	1.00	61.21
1107	C	TYR	663	48.565	6.680	51.537	1.00	59.94
1108	O	TYR	663	48.090	5.918	52.389	1.00	60.92
1109	N	LEU	664	48.930	6.274	50.325	1.00	60.84
1110	CA	LEU	664	48.846	4.881	49.908	1.00	61.56
1111	CB	LEU	664	49.261	4.757	48.438	1.00	60.37
1112	CG	LEU	664	48.363	5.402	47.382	1.00	64.33
1113	CD1	LEU	664	49.036	5.350	46.023	1.00	64.49
1114	CD2	LEU	664	47.032	4.687	47.351	1.00	59.02
1115	C	LEU	664	49.744	4.001	50.777	1.00	60.21
1116	O	LEU	664	49.369	2.889	51.161	1.00	61.89
1117	N	CYS	665	50.933	4.519	51.071	1.00	61.72
1118	CA	CYS	665	51.915	3.823	51.882	1.00	58.12
1119	CB	CYS	665	53.272	4.508	51.737	1.00	62.31
1120	SG	CYS	665	54.006	4.295	50.123	1.00	59.12
1121	C	CYS	665	51.516	3.771	53.348	1.00	59.84
1122	O	CYS	665	51.726	2.766	54.024	1.00	61.71
1123	N	MET	666	50.953	4.862	53.845	1.00	63.34
1124	CA	MET	666	50.524	4.910	55.228	1.00	58.59
1125	CB	MET	666	50.199	6.341	55.627	1.00	59.71
1126	CG	MET	666	51.408	7.189	55.867	1.00	62.55
1127	SD	MET	666	50.921	8.891	56.036	1.00	61.95
1128	CE	MET	666	50.313	8.927	57.659	1.00	64.15
1129	C	MET	666	49.303	4.023	55.437	1.00	63.86
1130	O	MET	666	49.146	3.420	56.495	1.00	59.48
1131	N	LYS	667	48.446	3.950	54.421	1.00	58.08
1132	CA	LYS	667	47.241	3.129	54.482	1.00	61.17
1133	CB	LYS	667	46.318	3.429	53.305	1.00	66.33
1134	CG	LYS	667	45.013	2.663	53.338	1.00	59.73
1135	CD	LYS	667	43.951	3.382	52.532	1.00	60.07
1136	CE	LYS	667	44.313	3.462	51.063	1.00	62.82
1137	NZ	LYS	667	44.134	2.158	50.390	1.00	62.44
1138	C	LYS	667	47.592	1.658	54.468	1.00	63.84
1139	O	LYS	667	46.867	0.838	55.011	1.00	61.95
1140	N	THR	668	48.705	1.318	53.838	1.00	63.32
1141	CA	THR	668	49.114	-0.069	53.801	1.00	61.88

1142	CB	THR	668	50.080	-0.304	52.657	1.00	60.27
1143	OG1	THR	668	49.463	0.124	51.439	1.00	62.16
1144	CG2	THR	668	50.417	-1.775	52.547	1.00	58.76
1145	C	THR	668	49.761	-0.413	55.137	1.00	62.68
1146	O	THR	668	49.707	-1.559	55.591	1.00	62.61
1147	N	LEU	669	50.350	0.597	55.773	1.00	62.26
1148	CA	LEU	669	50.995	0.427	57.068	1.00	61.58
1149	CB	LEU	669	51.888	1.626	57.378	1.00	62.50
1150	CG	LEU	669	53.265	1.643	56.712	1.00	57.56
1151	CD1	LEU	669	54.041	2.847	57.205	1.00	60.97
1152	CD2	LEU	669	54.012	0.355	57.037	1.00	59.22
1153	C	LEU	669	49.987	0.249	58.194	1.00	61.00
1154	O	LEU	669	50.354	-0.119	59.310	1.00	61.30
1155	N	LEU	670	48.718	0.520	57.911	1.00	62.31
1156	CA	LEU	670	47.686	0.365	58.925	1.00	62.17
1157	CB	LEU	670	46.511	1.305	58.638	1.00	64.37
1158	CG	LEU	670	46.784	2.784	58.942	1.00	60.87
1159	CD1	LEU	670	45.516	3.597	58.766	1.00	63.22
1160	CD2	LEU	670	47.293	2.922	60.365	1.00	58.85
1161	C	LEU	670	47.227	-1.090	58.976	1.00	63.40
1162	O	LEU	670	46.846	-1.599	60.026	1.00	63.58
1163	N	LEU	671	47.281	-1.750	57.827	1.00	61.89
1164	CA	LEU	671	46.913	-3.150	57.716	1.00	60.74
1165	CB	LEU	671	46.946	-3.574	56.249	1.00	62.54
1166	CG	LEU	671	46.501	-4.997	55.921	1.00	62.48
1167	CD1	LEU	671	45.015	-5.180	56.251	1.00	63.63
1168	CD2	LEU	671	46.768	-5.260	54.449	1.00	63.52
1169	C	LEU	671	47.967	-3.928	58.500	1.00	61.46
1170	O	LEU	671	47.688	-4.971	59.110	1.00	60.81
1171	N	LEU	672	49.182	-3.388	58.479	1.00	62.75
1172	CA	LEU	672	50.320	-3.974	59.163	1.00	62.92
1173	CB	LEU	672	51.562	-3.883	58.280	1.00	60.56
1174	CG	LEU	672	51.399	-4.164	56.786	1.00	62.90
1175	CD1	LEU	672	52.776	-4.394	56.183	1.00	60.90
1176	CD2	LEU	672	50.519	-5.373	56.558	1.00	61.77
1177	C	LEU	672	50.576	-3.232	60.468	1.00	61.14
1178	O	LEU	672	51.722	-3.064	60.883	1.00	63.28
1179	N	SER	673	49.502	-2.795	61.116	1.00	62.86
1180	CA	SER	673	49.616	-2.056	62.368	1.00	62.27
1181	CB	SER	673	48.582	-0.910	62.405	1.00	61.42
1182	OG	SER	673	47.241	-1.383	62.404	1.00	59.49
1183	C	SER	673	49.468	-2.925	63.616	1.00	63.23
1184	O	SER	673	50.026	-2.608	64.664	1.00	59.71
1185	N	SER	674	48.720	-4.017	63.517	1.00	61.92
1186	CA	SER	674	48.538	-4.875	64.680	1.00	60.38
1187	CB	SER	674	47.225	-4.506	65.401	1.00	62.70
1188	OG	SER	674	46.204	-4.115	64.495	1.00	56.91
1189	C	SER	674	48.590	-6.373	64.405	1.00	61.52

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1190	O	SER	674	48.122	-6.849	63.377	1.00	61.47
1191	N	VAL	675	49.192	-7.101	65.336	1.00	64.16
1192	CA	VAL	675	49.305	-8.556	65.256	1.00	61.09
1193	CB	VAL	675	50.722	-9.025	64.816	1.00	62.88
1194	CG1	VAL	675	50.962	-8.679	63.362	1.00	59.26
1195	CG2	VAL	675	51.787	-8.394	65.710	1.00	61.45
1196	C	VAL	675	49.039	-9.116	66.652	1.00	62.60
1197	O	VAL	675	49.265	-8.433	67.656	1.00	61.24
1198	N	PRO	676	48.550	-10.363	66.735	1.00	59.77
1199	CD	PRO	676	48.219	-11.265	65.616	1.00	57.51
1200	CA	PRO	676	48.260	-11.001	68.020	1.00	62.72
1201	CB	PRO	676	48.026	-12.452	67.623	1.00	60.61
1202	CG	PRO	676	47.362	-12.317	66.283	1.00	59.30
1203	C	PRO	676	49.424	-10.847	68.994	1.00	61.35
1204	O	PRO	676	50.585	-10.758	68.576	1.00	63.84
1205	N	LYS	677	49.117	-10.818	70.290	1.00	62.54
1206	CA	LYS	677	50.154	-10.673	71.314	1.00	60.54
1207	CB	LYS	677	49.510	-10.646	72.702	1.00	61.63
1208	CG	LYS	677	50.472	-10.433	73.853	1.00	58.65
1209	CD	LYS	677	49.861	-10.969	75.143	1.00	62.01
1210	CE	LYS	677	50.912	-11.109	76.241	1.00	63.79
1211	NZ	LYS	677	50.350	-11.727	77.491	1.00	60.49
1212	C	LYS	677	51.162	-11.828	71.222	1.00	61.45
1213	O	LYS	677	52.102	-11.917	72.023	1.00	59.62
1214	N	ASP	678	50.955	-12.698	70.231	1.00	59.93
1215	CA	ASP	678	51.809	-13.862	69.994	1.00	60.14
1216	CB	ASP	678	51.041	-15.126	70.367	1.00	60.09
1217	CG	ASP	678	50.390	-15.023	71.735	1.00	61.43
1218	OD1	ASP	678	51.110	-14.940	72.749	1.00	62.42
1219	OD2	ASP	678	49.151	-15.016	71.797	1.00	60.77
1220	C	ASP	678	52.273	-13.947	68.535	1.00	63.29
1221	O	ASP	678	52.771	-14.981	68.090	1.00	59.36
1222	N	GLY	679	52.098	-12.854	67.797	1.00	59.82
1223	CA	GLY	679	52.512	-12.823	66.408	1.00	58.14
1224	C	GLY	679	51.639	-13.640	65.481	1.00	58.50
1225	O	GLY	679	50.600	-14.179	65.870	1.00	58.88
1226	N	LEU	680	52.082	-13.723	64.237	1.00	62.95
1227	CA	LEU	680	51.375	-14.459	63.209	1.00	63.18
1228	CB	LEU	680	51.233	-13.564	61.981	1.00	65.44
1229	CG	LEU	680	50.941	-12.101	62.324	1.00	60.24
1230	CD1	LEU	680	50.994	-11.260	61.069	1.00	60.21
1231	CD2	LEU	680	49.582	-11.979	62.974	1.00	60.11
1232	C	LEU	680	52.221	-15.685	62.881	1.00	63.74
1233	O	LEU	680	53.430	-15.689	63.110	1.00	62.10
1234	N	LYS	681	51.598	-16.729	62.354	1.00	60.36
1235	CA	LYS	681	52.348	-17.922	62.000	1.00	60.78
1236	CB	LYS	681	51.406	-18.969	61.418	1.00	60.11
1237	CG	LYS	681	50.209	-19.253	62.289	1.00	61.43

1238	CD	LYS	681	49.295	-20.221	61.579	1.00	63.30
1239	CE	LYS	681	47.908	-20.186	62.160	1.00	61.77
1240	NZ	LYS	681	46.983	-20.886	61.244	1.00	62.13
1241	C	LYS	681	53.429	-17.551	60.973	1.00	61.58
1242	O	LYS	681	54.401	-18.286	60.784	1.00	63.01
1243	N	SER	682	53.250	-16.410	60.309	1.00	60.35
1244	CA	SER	682	54.211	-15.932	59.314	1.00	62.36
1245	CB	SER	682	53.515	-15.613	57.989	1.00	61.24
1246	OG	SER	682	53.066	-16.788	57.346	1.00	63.18
1247	C	SER	682	54.885	-14.674	59.826	1.00	64.68
1248	O	SER	682	55.289	-13.814	59.051	1.00	59.53
1249	N	GLN	683	55.012	-14.579	61.140	1.00	64.92
1250	CA	GLN	683	55.614	-13.411	61.754	1.00	62.89
1251	CB	GLN	683	55.862	-13.679	63.240	1.00	63.65
1252	CG	GLN	683	56.282	-12.452	64.059	1.00	64.38
1253	CD	GLN	683	55.318	-11.274	63.954	1.00	64.26
1254	OE1	GLN	683	55.688	-10.205	63.476	1.00	63.72
1255	NE2	GLN	683	54.085	-11.465	64.407	1.00	61.52
1256	C	GLN	683	56.893	-12.938	61.069	1.00	60.69
1257	O	GLN	683	56.981	-11.782	60.669	1.00	62.35
1258	N	GLU	684	57.880	-13.811	60.913	1.00	60.59
1259	CA	GLU	684	59.119	-13.378	60.279	1.00	61.72
1260	CB	GLU	684	60.039	-14.567	59.970	1.00	61.83
1261	CG	GLU	684	60.015	-15.013	58.511	1.00	61.93
1262	CD	GLU	684	61.383	-15.418	57.979	1.00	60.75
1263	OE1	GLU	684	61.457	-15.813	56.792	1.00	60.52
1264	OE2	GLU	684	62.375	-15.342	58.744	1.00	58.72
1265	C	GLU	684	58.801	-12.623	58.993	1.00	60.55
1266	O	GLU	684	59.196	-11.474	58.823	1.00	63.55
1267	N	LEU	685	58.064	-13.263	58.100	1.00	63.64
1268	CA	LEU	685	57.710	-12.649	56.834	1.00	57.80
1269	CB	LEU	685	56.921	-13.649	55.985	1.00	59.68
1270	CG	LEU	685	57.165	-13.734	54.476	1.00	63.20
1271	CD1	LEU	685	55.839	-14.063	53.829	1.00	59.43
1272	CD2	LEU	685	57.699	-12.434	53.902	1.00	62.25
1273	C	LEU	685	56.882	-11.370	57.040	1.00	62.31
1274	O	LEU	685	56.953	-10.432	56.242	1.00	61.77
1275	N	PHE	686	56.095	-11.326	58.109	1.00	60.23
1276	CA	PHE	686	55.272	-10.149	58.374	1.00	61.37
1277	CB	PHE	686	54.409	-10.365	59.609	1.00	64.14
1278	CG	PHE	686	53.663	-9.143	60.023	1.00	61.62
1279	CD1	PHE	686	52.639	-8.650	59.236	1.00	60.24
1280	CD2	PHE	686	54.008	-8.460	61.178	1.00	62.13
1281	CE1	PHE	686	51.971	-7.493	59.592	1.00	58.68
1282	CE2	PHE	686	53.347	-7.304	61.543	1.00	61.95
1283	CZ	PHE	686	52.326	-6.818	60.749	1.00	61.43
1284	C	PHE	686	56.109	-8.897	58.596	1.00	59.14
1285	O	PHE	686	56.247	-8.051	57.714	1.00	61.44

1286	N	ASP	687	56.651	-8.791	59.802	1.00	64.05
1287	CA	ASP	687	57.483	-7.668	60.195	1.00	60.85
1288	CB	ASP	687	58.102	-7.960	61.567	1.00	56.84
1289	CG	ASP	687	59.033	-9.162	61.536	1.00	64.67
1290	OD1	ASP	687	59.482	-9.610	62.622	1.00	60.21
1291	OD2	ASP	687	59.322	-9.655	60.414	1.00	63.02
1292	C	ASP	687	58.573	-7.383	59.142	1.00	61.59
1293	O	ASP	687	59.262	-6.358	59.214	1.00	61.60
1294	N	GLU	688	58.725	-8.289	58.172	1.00	60.82
1295	CA	GLU	688	59.700	-8.104	57.098	1.00	59.68
1296	CB	GLU	688	60.246	-9.433	56.604	1.00	62.54
1297	CG	GLU	688	61.434	-9.252	55.674	1.00	60.98
1298	CD	GLU	688	61.479	-10.289	54.569	1.00	58.58
1299	OE1	GLU	688	61.323	-9.898	53.387	1.00	61.73
1300	OE2	GLU	688	61.663	-11.490	54.882	1.00	60.24
1301	C	GLU	688	59.031	-7.387	55.931	1.00	60.97
1302	O	GLU	688	59.684	-6.719	55.137	1.00	62.27
1303	N	ILE	689	57.721	-7.552	55.809	1.00	61.23
1304	CA	ILE	689	56.979	-6.864	54.767	1.00	61.00
1305	CB	ILE	689	55.641	-7.592	54.451	1.00	63.41
1306	CG2	ILE	689	54.655	-6.650	53.759	1.00	59.25
1307	CG1	ILE	689	55.916	-8.808	53.568	1.00	57.54
1308	CD1	ILE	689	54.667	-9.526	53.121	1.00	62.29
1309	C	ILE	689	56.704	-5.479	55.345	1.00	58.97
1310	O	ILE	689	56.778	-4.473	54.645	1.00	61.54
1311	N	ARG	690	56.411	-5.439	56.641	1.00	60.16
1312	CA	ARG	690	56.135	-4.185	57.319	1.00	61.28
1313	CB	ARG	690	55.855	-4.434	58.799	1.00	60.29
1314	CG	ARG	690	55.548	-3.170	59.582	1.00	60.74
1315	CD	ARG	690	54.679	-3.480	60.770	1.00	56.91
1316	NE	ARG	690	54.190	-2.280	61.437	1.00	66.99
1317	CZ	ARG	690	54.967	-1.378	62.026	1.00	64.04
1318	NH1	ARG	690	56.283	-1.533	62.029	1.00	58.19
1319	NH2	ARG	690	54.427	-0.327	62.623	1.00	62.52
1320	C	ARG	690	57.274	-3.179	57.177	1.00	57.93
1321	O	ARG	690	57.037	-1.977	57.067	1.00	59.25
1322	N	MET	691	58.512	-3.660	57.190	1.00	58.75
1323	CA	MET	691	59.664	-2.783	57.048	1.00	64.96
1324	CB	MET	691	60.928	-3.542	57.450	1.00	61.53
1325	CG	MET	691	62.247	-3.016	56.886	1.00	59.40
1326	SD	MET	691	62.942	-4.201	55.673	1.00	61.45
1327	CE	MET	691	63.225	-5.669	56.764	1.00	60.93
1328	C	MET	691	59.775	-2.254	55.621	1.00	61.68
1329	O	MET	691	60.130	-1.099	55.405	1.00	63.95
1330	N	THR	692	59.459	-3.097	54.646	1.00	59.70
1331	CA	THR	692	59.519	-2.698	53.243	1.00	60.57
1332	CB	THR	692	59.105	-3.855	52.323	1.00	62.51
1333	OG1	THR	692	59.796	-5.046	52.714	1.00	59.90

1334	CG2	THR	692	59.437	-3.523	50.879	1.00	60.93
1335	C	THR	692	58.586	-1.523	52.962	1.00	60.46
1336	O	THR	692	58.890	-0.655	52.143	1.00	59.04
1337	N	TYR	693	57.439	-1.516	53.634	1.00	61.66
1338	CA	TYR	693	56.459	-0.458	53.461	1.00	60.32
1339	CB	TYR	693	55.045	-1.033	53.553	1.00	59.81
1340	CG	TYR	693	54.665	-1.802	52.302	1.00	61.04
1341	CD1	TYR	693	54.552	-1.153	51.073	1.00	63.46
1342	CE1	TYR	693	54.292	-1.865	49.909	1.00	65.96
1343	CD2	TYR	693	54.497	-3.185	52.332	1.00	59.82
1344	CE2	TYR	693	54.236	-3.906	51.170	1.00	63.54
1345	CZ	TYR	693	54.137	-3.242	49.967	1.00	62.96
1346	OH	TYR	693	53.901	-3.961	48.822	1.00	59.68
1347	C	TYR	693	56.663	0.664	54.458	1.00	58.94
1348	O	TYR	693	55.877	1.600	54.527	1.00	59.49
1349	N	ILE	694	57.720	0.555	55.248	1.00	63.16
1350	CA	ILE	694	58.052	1.598	56.195	1.00	61.35
1351	CB	ILE	694	58.734	1.042	57.462	1.00	59.89
1352	CG2	ILE	694	59.652	2.101	58.077	1.00	62.13
1353	CG1	ILE	694	57.668	0.580	58.457	1.00	63.95
1354	CD1	ILE	694	58.216	0.168	59.793	1.00	61.57
1355	C	ILE	694	59.028	2.478	55.430	1.00	58.86
1356	O	ILE	694	58.989	3.701	55.541	1.00	62.76
1357	N	LYS	695	59.890	1.838	54.643	1.00	61.80
1358	CA	LYS	695	60.869	2.539	53.821	1.00	60.19
1359	CB	LYS	695	61.987	1.607	53.364	1.00	61.05
1360	CG	LYS	695	62.768	0.892	54.438	1.00	60.54
1361	CD	LYS	695	63.876	0.081	53.767	1.00	63.44
1362	CE	LYS	695	64.516	-0.947	54.699	1.00	61.61
1363	NZ	LYS	695	65.330	-1.962	53.942	1.00	62.18
1364	C	LYS	695	60.206	3.074	52.559	1.00	61.44
1365	O	LYS	695	60.706	4.010	51.946	1.00	61.23
1366	N	GLU	696	59.101	2.452	52.156	1.00	61.65
1367	CA	GLU	696	58.381	2.862	50.961	1.00	60.70
1368	CB	GLU	696	57.289	1.851	50.635	1.00	62.74
1369	CG	GLU	696	56.806	1.901	49.200	1.00	63.74
1370	CD	GLU	696	57.927	1.725	48.187	1.00	63.24
1371	OE1	GLU	696	58.903	1.002	48.494	1.00	61.23
1372	OE2	GLU	696	57.824	2.299	47.079	1.00	62.98
1373	C	GLU	696	57.775	4.215	51.260	1.00	61.27
1374	O	GLU	696	57.594	5.051	50.366	1.00	61.63
1375	N	LEU	697	57.468	4.414	52.540	1.00	59.99
1376	CA	LEU	697	56.912	5.668	53.022	1.00	63.89
1377	CB	LEU	697	56.314	5.493	54.418	1.00	58.18
1378	CG	LEU	697	55.831	6.810	55.016	1.00	62.97
1379	CD1	LEU	697	54.754	7.370	54.127	1.00	59.80
1380	CD2	LEU	697	55.319	6.606	56.425	1.00	59.24
1381	C	LEU	697	58.029	6.709	53.072	1.00	61.66

1382	O	LEU	697	57.807	7.871	52.774	1.00	60.35
1383	N	GLY	698	59.228	6.283	53.460	1.00	59.57
1384	CA	GLY	698	60.348	7.198	53.523	1.00	61.15
1385	C	GLY	698	60.570	7.770	52.146	1.00	60.91
1386	O	GLY	698	60.748	8.977	51.988	1.00	61.15
1387	N	LYS	699	60.557	6.880	51.156	1.00	60.97
1388	CA	LYS	699	60.729	7.219	49.745	1.00	60.90
1389	CB	LYS	699	60.526	5.983	48.875	1.00	66.06
1390	CG	LYS	699	61.729	5.098	48.621	1.00	61.25
1391	CD	LYS	699	61.290	3.930	47.737	1.00	59.41
1392	CE	LYS	699	62.371	3.498	46.765	1.00	61.62
1393	NZ	LYS	699	63.066	2.246	47.178	1.00	60.87
1394	C	LYS	699	59.710	8.256	49.289	1.00	58.54
1395	O	LYS	699	60.019	9.127	48.482	1.00	59.98
1396	N	ALA	700	58.483	8.128	49.777	1.00	63.02
1397	CA	ALA	700	57.423	9.048	49.408	1.00	61.82
1398	CB	ALA	700	56.094	8.540	49.926	1.00	65.26
1399	C	ALA	700	57.712	10.422	49.977	1.00	60.36
1400	O	ALA	700	57.545	11.434	49.298	1.00	62.77
1401	N	ILE	701	58.137	10.446	51.235	1.00	65.16
1402	CA	ILE	701	58.471	11.683	51.917	1.00	64.84
1403	CB	ILE	701	58.931	11.406	53.338	1.00	61.36
1404	CG2	ILE	701	59.509	12.670	53.953	1.00	63.03
1405	CG1	ILE	701	57.761	10.874	54.151	1.00	61.61
1406	CD1	ILE	701	58.167	10.364	55.495	1.00	60.05
1407	C	ILE	701	59.574	12.455	51.195	1.00	61.64
1408	O	ILE	701	59.597	13.683	51.228	1.00	58.62
1409	N	VAL	702	60.500	11.749	50.555	1.00	63.95
1410	CA	VAL	702	61.560	12.438	49.831	1.00	57.69
1411	CB	VAL	702	62.815	11.532	49.665	1.00	63.59
1412	CG1	VAL	702	63.310	11.093	51.024	1.00	59.75
1413	CG2	VAL	702	62.494	10.330	48.819	1.00	64.22
1414	C	VAL	702	61.038	12.907	48.466	1.00	61.62
1415	O	VAL	702	61.328	14.014	48.031	1.00	61.64
1416	N	LYS	703	60.244	12.065	47.814	1.00	61.58
1417	CA	LYS	703	59.666	12.387	46.516	1.00	60.75
1418	CB	LYS	703	58.475	11.474	46.201	1.00	56.80
1419	CG	LYS	703	57.419	12.161	45.293	1.00	59.93
1420	CD	LYS	703	55.967	11.815	45.660	1.00	60.60
1421	CE	LYS	703	54.962	12.848	45.088	1.00	57.15
1422	NZ	LYS	703	55.070	13.064	43.605	1.00	62.62
1423	C	LYS	703	59.169	13.814	46.392	1.00	61.49
1424	O	LYS	703	59.454	14.472	45.404	1.00	58.34
1425	N	ARG	704	58.390	14.271	47.367	1.00	63.00
1426	CA	ARG	704	57.826	15.621	47.321	1.00	60.60
1427	CB	ARG	704	56.331	15.590	47.661	1.00	62.95
1428	CG	ARG	704	56.026	15.010	49.033	1.00	61.71
1429	CD	ARG	704	54.728	15.553	49.548	1.00	60.30

1430	NE	ARG	704	54.931	16.417	50.702	1.00	62.33
1431	CZ	ARG	704	53.983	17.200	51.204	1.00	60.19
1432	NH1	ARG	704	52.784	17.213	50.640	1.00	61.68
1433	NH2	ARG	704	54.225	17.965	52.263	1.00	63.26
1434	C	ARG	704	58.520	16.607	48.249	1.00	63.14
1435	O	ARG	704	58.732	17.772	47.885	1.00	60.41
1436	N	GLU	705	58.842	16.155	49.458	1.00	60.89
1437	CA	GLU	705	59.528	17.018	50.412	1.00	62.58
1438	CB	GLU	705	59.814	16.288	51.730	1.00	60.91
1439	CG	GLU	705	58.605	16.091	52.605	1.00	62.30
1440	CD	GLU	705	57.847	17.384	52.817	1.00	64.22
1441	OE1	GLU	705	56.684	17.460	52.347	1.00	58.55
1442	OE2	GLU	705	58.419	18.317	53.440	1.00	61.42
1443	C	GLU	705	60.848	17.456	49.801	1.00	62.10
1444	O	GLU	705	61.869	16.761	49.939	1.00	59.78
1445	N	GLY	706	60.823	18.597	49.115	1.00	60.22
1446	CA	GLY	706	62.036	19.100	48.500	1.00	61.75
1447	C	GLY	706	63.159	19.239	49.518	1.00	60.44
1448	O	GLY	706	64.168	18.519	49.450	1.00	61.54
1449	N	ASN	707	62.974	20.148	50.477	1.00	61.06
1450	CA	ASN	707	63.989	20.387	51.491	1.00	60.61
1451	CB	ASN	707	63.561	21.505	52.443	1.00	63.06
1452	CG	ASN	707	64.731	22.048	53.258	1.00	60.50
1453	OD1	ASN	707	64.663	23.152	53.803	1.00	61.18
1454	ND2	ASN	707	65.815	21.269	53.342	1.00	61.75
1455	C	ASN	707	64.355	19.143	52.281	1.00	61.56
1456	O	ASN	707	63.685	18.767	53.250	1.00	63.56
1457	N	SER	708	65.446	18.525	51.837	1.00	62.02
1458	CA	SER	708	66.024	17.326	52.427	1.00	60.22
1459	CB	SER	708	67.379	17.070	51.737	1.00	58.91
1460	OG	SER	708	68.112	15.998	52.305	1.00	62.15
1461	C	SER	708	66.200	17.500	53.945	1.00	63.60
1462	O	SER	708	66.754	16.635	54.624	1.00	60.95
1463	N	SER	709	65.713	18.619	54.474	1.00	61.83
1464	CA	SER	709	65.826	18.922	55.894	1.00	61.35
1465	CB	SER	709	66.279	20.373	56.065	1.00	65.65
1466	OG	SER	709	67.479	20.615	55.332	1.00	62.14
1467	C	SER	709	64.516	18.684	56.641	1.00	59.54
1468	O	SER	709	64.497	18.583	57.874	1.00	61.29
1469	N	GLN	710	63.416	18.586	55.900	1.00	62.57
1470	CA	GLN	710	62.131	18.347	56.533	1.00	61.59
1471	CB	GLN	710	61.087	19.333	56.007	1.00	58.05
1472	CG	GLN	710	61.469	20.792	56.249	1.00	62.98
1473	CD	GLN	710	60.344	21.776	55.943	1.00	59.84
1474	OE1	GLN	710	59.363	21.882	56.696	1.00	60.97
1475	NE2	GLN	710	60.481	22.502	54.831	1.00	65.14
1476	C	GLN	710	61.683	16.917	56.297	1.00	58.31
1477	O	GLN	710	60.512	16.586	56.466	1.00	60.42

1478	N	ASN	711	62.625	16.063	55.916	1.00	61.21
1479	CA	ASN	711	62.309	14.666	55.673	1.00	63.02
1480	CB	ASN	711	63.407	14.033	54.819	1.00	60.49
1481	CG	ASN	711	63.508	14.675	53.449	1.00	65.80
1482	OD1	ASN	711	62.565	15.303	52.977	1.00	63.88
1483	ND2	ASN	711	64.646	14.507	52.801	1.00	60.91
1484	C	ASN	711	62.090	13.879	56.974	1.00	63.26
1485	O	ASN	711	61.055	13.238	57.155	1.00	58.14
1486	N	TRP	712	63.054	13.930	57.883	1.00	61.93
1487	CA	TRP	712	62.915	13.234	59.148	1.00	59.49
1488	CB	TRP	712	64.259	13.185	59.833	1.00	62.44
1489	CG	TRP	712	65.169	12.333	59.088	1.00	62.60
1490	CD2	TRP	712	65.485	10.980	59.388	1.00	61.74
1491	CE2	TRP	712	66.331	10.516	58.366	1.00	62.04
1492	CE3	TRP	712	65.130	10.108	60.426	1.00	60.92
1493	CD1	TRP	712	65.815	12.637	57.934	1.00	57.10
1494	NE1	TRP	712	66.517	11.552	57.490	1.00	63.63
1495	CZ2	TRP	712	66.832	9.215	58.345	1.00	63.94
1496	CZ3	TRP	712	65.625	8.817	60.407	1.00	65.64
1497	CH2	TRP	712	66.470	8.381	59.370	1.00	62.08
1498	C	TRP	712	61.903	13.954	60.021	1.00	59.14
1499	O	TRP	712	61.372	13.410	60.996	1.00	59.32
1500	N	GLN	713	61.637	15.191	59.640	1.00	60.06
1501	CA	GLN	713	60.705	16.043	60.345	1.00	63.93
1502	CB	GLN	713	60.853	17.455	59.793	1.00	59.11
1503	CG	GLN	713	60.727	18.564	60.802	1.00	61.74
1504	CD	GLN	713	59.352	19.135	60.838	1.00	60.27
1505	OE1	GLN	713	58.660	19.154	59.824	1.00	58.27
1506	NE2	GLN	713	58.942	19.628	61.998	1.00	65.68
1507	C	GLN	713	59.296	15.522	60.107	1.00	57.87
1508	O	GLN	713	58.472	15.465	61.018	1.00	63.21
1509	N	ARG	714	59.051	15.125	58.864	1.00	62.15
1510	CA	ARG	714	57.758	14.626	58.424	1.00	57.88
1511	CB	ARG	714	57.668	14.782	56.907	1.00	65.30
1512	CG	ARG	714	56.272	14.971	56.382	1.00	62.96
1513	CD	ARG	714	56.301	15.439	54.940	1.00	62.68
1514	NE	ARG	714	55.029	15.200	54.267	1.00	62.08
1515	CZ	ARG	714	53.899	15.828	54.561	1.00	62.26
1516	NH1	ARG	714	53.877	16.741	55.515	1.00	59.12
1517	NH2	ARG	714	52.788	15.535	53.906	1.00	57.33
1518	C	ARG	714	57.573	13.171	58.831	1.00	60.95
1519	O	ARG	714	56.531	12.787	59.368	1.00	60.00
1520	N	PHE	715	58.594	12.363	58.571	1.00	59.93
1521	CA	PHE	715	58.551	10.960	58.940	1.00	61.38
1522	CB	PHE	715	59.934	10.328	58.799	1.00	60.45
1523	CG	PHE	715	59.921	8.834	58.843	1.00	63.37
1524	CD1	PHE	715	59.016	8.119	58.063	1.00	61.57
1525	CD2	PHE	715	60.824	8.136	59.636	1.00	59.17

1526	CE1	PHE	715	59.005	6.732	58.067	1.00	60.07
1527	CE2	PHE	715	60.824	6.740	59.648	1.00	58.03
1528	CZ	PHE	715	59.904	6.038	58.856	1.00	61.29
1529	C	PHE	715	58.118	10.923	60.394	1.00	61.16
1530	O	PHE	715	57.409	10.017	60.821	1.00	61.52
1531	N	TYR	716	58.541	11.925	61.153	1.00	62.10
1532	CA	TYR	716	58.178	11.989	62.550	1.00	61.74
1533	CB	TYR	716	58.962	13.092	63.256	1.00	60.58
1534	CG	TYR	716	58.729	13.117	64.748	1.00	60.86
1535	CD1	TYR	716	59.376	12.213	65.586	1.00	58.32
1536	CE1	TYR	716	59.159	12.226	66.952	1.00	59.67
1537	CD2	TYR	716	57.852	14.032	65.318	1.00	60.64
1538	CE2	TYR	716	57.625	14.052	66.679	1.00	63.17
1539	CZ	TYR	716	58.283	13.152	67.493	1.00	58.37
1540	OH	TYR	716	58.090	13.194	68.856	1.00	59.28
1541	C	TYR	716	56.688	12.280	62.662	1.00	61.28
1542	O	TYR	716	55.952	11.578	63.356	1.00	61.70
1543	N	GLN	717	56.249	13.318	61.967	1.00	62.49
1544	CA	GLN	717	54.858	13.716	62.009	1.00	63.77
1545	CB	GLN	717	54.694	15.061	61.304	1.00	63.18
1546	CG	GLN	717	55.613	16.126	61.888	1.00	62.93
1547	CD	GLN	717	55.418	17.512	61.288	1.00	62.21
1548	OE1	GLN	717	55.545	17.709	60.073	1.00	59.68
1549	NE2	GLN	717	55.125	18.487	62.147	1.00	58.70
1550	C	GLN	717	53.910	12.674	61.426	1.00	61.09
1551	O	GLN	717	52.907	12.338	62.064	1.00	61.62
1552	N	LEU	718	54.228	12.154	60.237	1.00	62.25
1553	CA	LEU	718	53.384	11.144	59.589	1.00	60.93
1554	CB	LEU	718	53.880	10.833	58.166	1.00	61.18
1555	CG	LEU	718	53.823	11.915	57.078	1.00	60.69
1556	CD1	LEU	718	54.322	11.353	55.764	1.00	59.94
1557	CD2	LEU	718	52.411	12.419	56.916	1.00	64.72
1558	C	LEU	718	53.308	9.847	60.391	1.00	61.41
1559	O	LEU	718	52.241	9.270	60.530	1.00	62.27
1560	N	THR	719	54.441	9.387	60.911	1.00	62.60
1561	CA	THR	719	54.469	8.162	61.706	1.00	61.77
1562	CB	THR	719	55.902	7.717	62.001	1.00	63.38
1563	OG1	THR	719	56.590	8.749	62.715	1.00	59.25
1564	CG2	THR	719	56.626	7.420	60.716	1.00	64.41
1565	C	THR	719	53.744	8.362	63.034	1.00	64.18
1566	O	THR	719	53.365	7.398	63.702	1.00	59.43
1567	N	LYS	720	53.562	9.619	63.421	1.00	60.48
1568	CA	LYS	720	52.864	9.913	64.652	1.00	60.21
1569	CB	LYS	720	53.414	11.194	65.281	1.00	63.61
1570	CG	LYS	720	52.661	11.630	66.532	1.00	60.31
1571	CD	LYS	720	52.340	10.450	67.448	1.00	57.45
1572	CE	LYS	720	51.254	10.801	68.472	1.00	57.33
1573	NZ	LYS	720	50.621	9.562	69.037	1.00	61.89

1574	C	LYS	720	51.364	10.023	64.345	1.00	60.76
1575	O	LYS	720	50.523	10.016	65.246	1.00	60.43
1576	N	LEU	721	51.030	10.110	63.061	1.00	65.16
1577	CA	LEU	721	49.634	10.162	62.659	1.00	59.83
1578	CB	LEU	721	49.505	10.724	61.235	1.00	59.18
1579	CG	LEU	721	48.264	11.548	60.867	1.00	63.18
1580	CD1	LEU	721	48.219	11.751	59.366	1.00	62.00
1581	CD2	LEU	721	47.005	10.851	61.327	1.00	62.08
1582	C	LEU	721	49.163	8.696	62.703	1.00	61.87
1583	O	LEU	721	48.041	8.405	63.117	1.00	62.35
1584	N	LEU	722	50.052	7.788	62.282	1.00	62.99
1585	CA	LEU	722	49.813	6.339	62.250	1.00	58.34
1586	CB	LEU	722	50.988	5.635	61.570	1.00	59.92
1587	CG	LEU	722	51.194	5.933	60.084	1.00	60.23
1588	CD1	LEU	722	52.500	5.333	59.636	1.00	58.33
1589	CD2	LEU	722	50.050	5.373	59.264	1.00	59.18
1590	C	LEU	722	49.624	5.754	63.651	1.00	62.26
1591	O	LEU	722	48.827	4.835	63.860	1.00	60.80
1592	N	ASP	723	50.389	6.282	64.597	1.00	60.29
1593	CA	ASP	723	50.321	5.870	65.989	1.00	61.98
1594	CB	ASP	723	51.409	6.583	66.780	1.00	62.74
1595	CG	ASP	723	52.652	5.759	66.935	1.00	62.09
1596	OD1	ASP	723	52.840	4.814	66.146	1.00	62.64
1597	OD2	ASP	723	53.445	6.066	67.848	1.00	60.13
1598	C	ASP	723	48.970	6.275	66.554	1.00	61.71
1599	O	ASP	723	48.281	5.496	67.202	1.00	61.64
1600	N	SER	724	48.612	7.524	66.305	1.00	62.20
1601	CA	SER	724	47.362	8.090	66.784	1.00	61.12
1602	CB	SER	724	47.329	9.579	66.449	1.00	63.08
1603	OG	SER	724	47.513	9.767	65.057	1.00	61.03
1604	C	SER	724	46.098	7.419	66.246	1.00	59.27
1605	O	SER	724	45.015	7.664	66.772	1.00	61.79
1606	N	MET	725	46.229	6.594	65.203	1.00	60.63
1607	CA	MET	725	45.077	5.893	64.615	1.00	60.05
1608	CB	MET	725	45.425	5.228	63.272	1.00	60.16
1609	CG	MET	725	45.452	6.151	62.055	1.00	66.62
1610	SD	MET	725	43.992	7.180	61.838	1.00	58.95
1611	CE	MET	725	42.904	6.134	61.000	1.00	61.36
1612	C	MET	725	44.573	4.833	65.576	1.00	64.25
1613	O	MET	725	43.382	4.543	65.627	1.00	59.89
1614	N	HIS	726	45.492	4.251	66.334	1.00	62.22
1615	CA	HIS	726	45.122	3.249	67.313	1.00	60.86
1616	CB	HIS	726	46.356	2.746	68.064	1.00	58.90
1617	CG	HIS	726	47.183	1.772	67.286	1.00	59.73
1618	CD2	HIS	726	48.518	1.706	67.070	1.00	60.15
1619	ND1	HIS	726	46.635	0.682	66.646	1.00	61.70
1620	CE1	HIS	726	47.598	-0.014	66.069	1.00	61.05
1621	NE2	HIS	726	48.750	0.586	66.311	1.00	60.76

1622	C	HIS	726	44.141	3.880	68.291	1.00	61.09
1623	O	HIS	726	43.146	3.268	68.650	1.00	60.43
1624	N	GLU	727	44.425	5.109	68.714	1.00	61.91
1625	CA	GLU	727	43.548	5.825	69.642	1.00	58.28
1626	CB	GLU	727	44.218	7.109	70.159	1.00	63.92
1627	CG	GLU	727	43.254	8.102	70.846	1.00	59.43
1628	CD	GLU	727	43.073	9.413	70.053	1.00	61.79
1629	OE1	GLU	727	44.079	10.150	69.874	1.00	60.96
1630	OE2	GLU	727	41.931	9.707	69.607	1.00	63.98
1631	C	GLU	727	42.220	6.187	68.993	1.00	60.97
1632	O	GLU	727	41.163	6.009	69.596	1.00	58.72
1633	N	VAL	728	42.263	6.699	67.769	1.00	60.50
1634	CA	VAL	728	41.022	7.073	67.105	1.00	60.74
1635	CB	VAL	728	41.289	7.922	65.828	1.00	58.90
1636	CG1	VAL	728	42.719	7.804	65.415	1.00	58.73
1637	CG2	VAL	728	40.382	7.494	64.703	1.00	65.58
1638	C	VAL	728	40.192	5.842	66.773	1.00	59.91
1639	O	VAL	728	38.971	5.844	66.931	1.00	61.17
1640	N	VAL	729	40.872	4.792	66.326	1.00	61.77
1641	CA	VAL	729	40.243	3.522	65.974	1.00	62.39
1642	CB	VAL	729	41.277	2.578	65.332	1.00	60.27
1643	CG1	VAL	729	40.946	1.131	65.606	1.00	61.53
1644	CG2	VAL	729	41.298	2.815	63.866	1.00	60.01
1645	C	VAL	729	39.586	2.830	67.173	1.00	61.69
1646	O	VAL	729	38.718	1.971	67.009	1.00	59.65
1647	N	GLU	730	39.999	3.199	68.377	1.00	59.90
1648	CA	GLU	730	39.411	2.601	69.558	1.00	60.27
1649	CB	GLU	730	40.308	2.812	70.755	1.00	59.45
1650	CG	GLU	730	39.878	2.014	71.942	1.00	66.48
1651	CD	GLU	730	40.681	2.348	73.167	1.00	62.84
1652	OE1	GLU	730	41.912	2.547	73.039	1.00	61.03
1653	OE2	GLU	730	40.081	2.400	74.263	1.00	60.34
1654	C	GLU	730	38.085	3.291	69.804	1.00	62.24
1655	O	GLU	730	37.031	2.660	69.869	1.00	60.10
1656	N	ASN	731	38.154	4.606	69.941	1.00	61.01
1657	CA	ASN	731	36.967	5.409	70.157	1.00	60.41
1658	CB	ASN	731	37.356	6.880	70.212	1.00	62.98
1659	CG	ASN	731	37.593	7.333	71.613	1.00	59.54
1660	OD1	ASN	731	36.657	7.385	72.410	1.00	58.59
1661	ND2	ASN	731	38.841	7.638	71.945	1.00	58.18
1662	C	ASN	731	35.917	5.165	69.081	1.00	61.30
1663	O	ASN	731	34.720	5.345	69.317	1.00	60.95
1664	N	LEU	732	36.364	4.750	67.902	1.00	60.39
1665	CA	LEU	732	35.442	4.475	66.820	1.00	61.55
1666	CB	LEU	732	36.141	4.550	65.471	1.00	59.24
1667	CG	LEU	732	36.184	5.931	64.813	1.00	64.00
1668	CD1	LEU	732	36.712	5.787	63.374	1.00	62.90
1669	CD2	LEU	732	34.771	6.561	64.818	1.00	60.26

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1670	C	LEU	732	34.841	3.108	66.997	1.00	60.27
1671	O	LEU	732	33.648	2.922	66.774	1.00	61.79
1672	N	LEU	733	35.673	2.148	67.399	1.00	58.72
1673	CA	LEU	733	35.214	0.770	67.612	1.00	60.63
1674	CB	LEU	733	36.376	-0.153	67.969	1.00	60.85
1675	CG	LEU	733	37.087	-0.798	66.782	1.00	56.83
1676	CD1	LEU	733	38.344	-1.474	67.266	1.00	63.66
1677	CD2	LEU	733	36.159	-1.786	66.083	1.00	56.09
1678	C	LEU	733	34.158	0.663	68.696	1.00	60.11
1679	O	LEU	733	33.092	0.098	68.458	1.00	60.20
1680	N	ASN	734	34.456	1.192	69.883	1.00	64.88
1681	CA	ASN	734	33.503	1.148	70.988	1.00	60.87
1682	CB	ASN	734	33.874	2.130	72.099	1.00	64.42
1683	CG	ASN	734	35.076	1.683	72.896	1.00	60.85
1684	OD1	ASN	734	35.499	0.526	72.817	1.00	60.20
1685	ND2	ASN	734	35.627	2.597	73.686	1.00	62.04
1686	C	ASN	734	32.157	1.544	70.455	1.00	59.98
1687	O	ASN	734	31.209	0.755	70.478	1.00	59.10
1688	N	TYR	735	32.085	2.778	69.969	1.00	61.85
1689	CA	TYR	735	30.844	3.294	69.421	1.00	63.27
1690	CB	TYR	735	31.075	4.640	68.743	1.00	60.68
1691	CG	TYR	735	29.867	5.515	68.853	1.00	62.56
1692	CD1	TYR	735	28.777	5.328	67.975	1.00	60.84
1693	CE1	TYR	735	27.586	6.030	68.168	1.00	60.10
1694	CD2	TYR	735	29.722	6.421	69.889	1.00	62.93
1695	CE2	TYR	735	28.543	7.127	70.084	1.00	62.59
1696	CZ	TYR	735	27.483	6.916	69.221	1.00	60.99
1697	OH	TYR	735	26.305	7.561	69.418	1.00	56.15
1698	C	TYR	735	30.261	2.306	68.418	1.00	57.10
1699	O	TYR	735	29.052	2.158	68.321	1.00	60.19
1700	N	CYS	736	31.126	1.621	67.682	1.00	62.53
1701	CA	CYS	736	30.673	0.644	66.707	1.00	60.21
1702	CB	CYS	736	31.842	0.208	65.815	1.00	62.29
1703	SG	CYS	736	31.461	-1.142	64.660	1.00	62.77
1704	C	CYS	736	30.063	-0.572	67.399	1.00	62.99
1705	O	CYS	736	28.857	-0.795	67.290	1.00	61.76
1706	N	PHE	737	30.892	-1.346	68.111	1.00	60.76
1707	CA	PHE	737	30.435	-2.546	68.835	1.00	61.61
1708	CB	PHE	737	31.454	-3.013	69.889	1.00	65.67
1709	CG	PHE	737	32.718	-3.575	69.321	1.00	61.17
1710	CD1	PHE	737	32.732	-4.173	68.069	1.00	62.43
1711	CD2	PHE	737	33.904	-3.515	70.049	1.00	62.09
1712	CE1	PHE	737	33.908	-4.704	67.544	1.00	60.80
1713	CE2	PHE	737	35.083	-4.042	69.536	1.00	61.51
1714	CZ	PHE	737	35.086	-4.638	68.279	1.00	59.32
1715	C	PHE	737	29.151	-2.266	69.581	1.00	60.98
1716	O	PHE	737	28.103	-2.865	69.312	1.00	61.98
1717	N	GLN	738	29.274	-1.356	70.542	1.00	64.21

1718	CA	GLN	738	28.183	-0.934	71.399	1.00	63.22
1719	CB	GLN	738	28.613	0.301	72.173	1.00	64.29
1720	CG	GLN	738	27.542	0.896	73.021	1.00	59.02
1721	CD	GLN	738	27.555	2.392	72.920	1.00	61.20
1722	OE1	GLN	738	27.116	2.962	71.916	1.00	60.80
1723	NE2	GLN	738	28.082	3.048	73.948	1.00	57.12
1724	C	GLN	738	26.917	-0.640	70.606	1.00	61.18
1725	O	GLN	738	25.827	-1.017	71.009	1.00	61.34
1726	N	THR	739	27.056	0.037	69.478	1.00	61.45
1727	CA	THR	739	25.893	0.326	68.678	1.00	60.85
1728	CB	THR	739	26.208	1.297	67.542	1.00	55.90
1729	OG1	THR	739	26.212	2.649	68.047	1.00	60.51
1730	CG2	THR	739	25.193	1.200	66.444	1.00	62.24
1731	C	THR	739	25.330	-0.969	68.085	1.00	62.53
1732	O	THR	739	24.122	-1.107	67.898	1.00	60.85
1733	N	PHE	740	26.221	-1.906	67.784	1.00	61.25
1734	CA	PHE	740	25.859	-3.197	67.215	1.00	59.86
1735	CB	PHE	740	27.110	-3.854	66.641	1.00	60.28
1736	CG	PHE	740	26.937	-5.301	66.311	1.00	63.82
1737	CD1	PHE	740	26.434	-5.690	65.079	1.00	62.86
1738	CD2	PHE	740	27.297	-6.278	67.236	1.00	61.71
1739	CE1	PHE	740	26.295	-7.042	64.763	1.00	60.86
1740	CE2	PHE	740	27.165	-7.623	66.938	1.00	60.83
1741	CZ	PHE	740	26.663	-8.013	65.696	1.00	60.77
1742	C	PHE	740	25.200	-4.140	68.238	1.00	60.76
1743	O	PHE	740	24.420	-5.028	67.866	1.00	60.72
1744	N	LEU	741	25.538	-3.965	69.515	1.00	62.82
1745	CA	LEU	741	24.976	-4.793	70.584	1.00	61.57
1746	CB	LEU	741	25.991	-5.012	71.708	1.00	59.14
1747	CG	LEU	741	27.187	-5.904	71.404	1.00	62.48
1748	CD1	LEU	741	28.083	-5.956	72.627	1.00	58.13
1749	CD2	LEU	741	26.708	-7.294	71.021	1.00	60.31
1750	C	LEU	741	23.770	-4.087	71.165	1.00	60.19
1751	O	LEU	741	23.577	-4.055	72.389	1.00	59.64
1752	N	ASP	742	22.960	-3.508	70.290	1.00	61.92
1753	CA	ASP	742	21.789	-2.797	70.762	1.00	60.22
1754	CB	ASP	742	22.185	-1.372	71.179	1.00	61.70
1755	CG	ASP	742	21.021	-0.598	71.793	1.00	60.82
1756	OD1	ASP	742	21.258	0.438	72.473	1.00	60.77
1757	OD2	ASP	742	19.863	-1.028	71.587	1.00	61.09
1758	C	ASP	742	20.689	-2.769	69.710	1.00	61.90
1759	O	ASP	742	20.530	-1.782	68.995	1.00	61.23
1760	N	LYS	743	19.934	-3.864	69.623	1.00	63.29
1761	CA	LYS	743	18.833	-3.975	68.664	1.00	62.18
1762	CB	LYS	743	18.045	-5.273	68.888	1.00	63.55
1763	CG	LYS	743	18.054	-6.243	67.705	1.00	62.77
1764	CD	LYS	743	17.301	-5.691	66.489	1.00	59.38
1765	CE	LYS	743	17.291	-6.724	65.349	1.00	62.80

1766	NZ	LYS	743	16.446	-6.335	64.166	1.00	57.45
1767	C	LYS	743	17.899	-2.786	68.822	1.00	62.93
1768	O	LYS	743	17.407	-2.248	67.833	1.00	58.22
1769	N	THR	744	17.669	-2.383	70.069	1.00	61.23
1770	CA	THR	744	16.808	-1.247	70.400	1.00	61.48
1771	CB	THR	744	17.148	-0.715	71.802	1.00	63.18
1772	OG1	THR	744	17.199	-1.817	72.719	1.00	59.84
1773	CG2	THR	744	16.112	0.308	72.265	1.00	60.98
1774	C	THR	744	16.913	-0.077	69.411	1.00	59.67
1775	O	THR	744	15.913	0.580	69.118	1.00	64.20
1776	N	MET	745	18.117	0.184	68.903	1.00	61.36
1777	CA	MET	745	18.322	1.282	67.961	1.00	62.05
1778	CB	MET	745	19.703	1.909	68.158	1.00	63.01
1779	CG	MET	745	20.029	2.189	69.614	1.00	61.21
1780	SD	MET	745	21.418	3.324	69.877	1.00	62.14
1781	CE	MET	745	20.934	4.087	71.538	1.00	61.78
1782	C	MET	745	18.175	0.824	66.517	1.00	59.56
1783	O	MET	745	18.382	1.605	65.585	1.00	62.58
1784	N	SER	746	17.817	-0.442	66.334	1.00	59.78
1785	CA	SER	746	17.624	-1.000	64.996	1.00	58.09
1786	CB	SER	746	16.169	-0.786	64.541	1.00	58.34
1787	OG	SER	746	15.252	-1.368	65.455	1.00	63.83
1788	C	SER	746	18.592	-0.429	63.940	1.00	59.09
1789	O	SER	746	18.176	0.027	62.867	1.00	61.57
1790	N	ILE	747	19.882	-0.432	64.269	1.00	62.10
1791	CA	ILE	747	20.905	0.022	63.342	1.00	61.22
1792	CB	ILE	747	22.021	0.814	64.054	1.00	63.05
1793	CG2	ILE	747	23.241	0.930	63.145	1.00	64.60
1794	CG1	ILE	747	21.499	2.205	64.426	1.00	61.38
1795	CD1	ILE	747	22.576	3.198	64.804	1.00	63.35
1796	C	ILE	747	21.465	-1.260	62.749	1.00	62.54
1797	O	ILE	747	22.169	-2.011	63.419	1.00	60.09
1798	N	GLU	748	21.125	-1.507	61.491	1.00	60.25
1799	CA	GLU	748	21.541	-2.711	60.787	1.00	60.97
1800	CB	GLU	748	20.497	-3.038	59.709	1.00	63.45
1801	CG	GLU	748	20.877	-4.168	58.756	1.00	60.81
1802	CD	GLU	748	19.678	-4.723	57.973	1.00	59.13
1803	OE1	GLU	748	19.013	-3.932	57.262	1.00	62.39
1804	OE2	GLU	748	19.406	-5.950	58.072	1.00	61.13
1805	C	GLU	748	22.940	-2.658	60.175	1.00	61.28
1806	O	GLU	748	23.391	-1.616	59.690	1.00	62.62
1807	N	PHE	749	23.622	-3.800	60.231	1.00	62.73
1808	CA	PHE	749	24.963	-3.959	59.667	1.00	59.35
1809	CB	PHE	749	25.974	-4.421	60.733	1.00	59.45
1810	CG	PHE	749	26.299	-3.389	61.759	1.00	64.74
1811	CD1	PHE	749	25.399	-3.085	62.770	1.00	59.18
1812	CD2	PHE	749	27.514	-2.721	61.721	1.00	57.96
1813	CE1	PHE	749	25.708	-2.119	63.742	1.00	61.52

1814	CE2	PHE	749	27.839	-1.753	62.685	1.00	65.31
1815	CZ	PHE	749	26.934	-1.451	63.697	1.00	59.87
1816	C	PHE	749	24.872	-5.048	58.599	1.00	60.75
1817	O	PHE	749	24.047	-5.952	58.705	1.00	62.03
1818	N	PRO	750	25.705	-4.970	57.550	1.00	61.23
1819	CD	PRO	750	26.645	-3.910	57.166	1.00	60.04
1820	CA	PRO	750	25.652	-6.003	56.516	1.00	61.34
1821	CB	PRO	750	26.584	-5.468	55.434	1.00	64.04
1822	CG	PRO	750	26.608	-4.015	55.668	1.00	60.17
1823	C	PRO	750	26.240	-7.235	57.172	1.00	60.83
1824	O	PRO	750	26.788	-7.143	58.271	1.00	59.53
1825	N	GLU	751	26.139	-8.386	56.523	1.00	60.43
1826	CA	GLU	751	26.719	-9.572	57.122	1.00	61.33
1827	CB	GLU	751	26.350	-10.834	56.311	1.00	62.90
1828	CG	GLU	751	25.560	-10.608	55.002	1.00	60.51
1829	CD	GLU	751	26.436	-10.142	53.837	1.00	57.86
1830	OE1	GLU	751	27.420	-10.844	53.519	1.00	60.97
1831	OE2	GLU	751	26.138	-9.084	53.240	1.00	59.16
1832	C	GLU	751	28.255	-9.389	57.219	1.00	58.48
1833	O	GLU	751	28.850	-9.561	58.292	1.00	59.47
1834	N	MET	752	28.891	-9.004	56.115	1.00	64.26
1835	CA	MET	752	30.336	-8.808	56.109	1.00	61.15
1836	CB	MET	752	30.777	-8.060	54.857	1.00	63.84
1837	CG	MET	752	32.255	-7.666	54.898	1.00	64.44
1838	SD	MET	752	33.383	-9.076	55.043	1.00	67.15
1839	CE	MET	752	33.649	-9.386	53.307	1.00	59.96
1840	C	MET	752	30.884	-8.072	57.323	1.00	62.38
1841	O	MET	752	31.963	-8.394	57.811	1.00	60.81
1842	N	LEU	753	30.163	-7.067	57.796	1.00	59.19
1843	CA	LEU	753	30.627	-6.323	58.957	1.00	62.39
1844	CB	LEU	753	30.187	-4.862	58.881	1.00	61.65
1845	CG	LEU	753	31.214	-3.835	58.397	1.00	61.49
1846	CD1	LEU	753	31.713	-4.171	57.010	1.00	61.11
1847	CD2	LEU	753	30.567	-2.471	58.411	1.00	63.29
1848	C	LEU	753	30.114	-6.946	60.241	1.00	58.84
1849	O	LEU	753	30.779	-6.885	61.273	1.00	61.39
1850	N	ALA	754	28.927	-7.541	60.177	1.00	62.56
1851	CA	ALA	754	28.337	-8.194	61.343	1.00	61.99
1852	CB	ALA	754	26.963	-8.775	60.983	1.00	59.37
1853	C	ALA	754	29.287	-9.313	61.747	1.00	66.01
1854	O	ALA	754	29.619	-9.482	62.922	1.00	63.54
1855	N	GLU	755	29.724	-10.044	60.722	1.00	63.92
1856	CA	GLU	755	30.632	-11.194	60.795	1.00	59.42
1857	CB	GLU	755	30.674	-11.851	59.407	1.00	60.24
1858	CG	GLU	755	31.733	-12.933	59.190	1.00	62.29
1859	CD	GLU	755	31.348	-14.260	59.811	1.00	59.60
1860	OE1	GLU	755	30.318	-14.834	59.388	1.00	60.67
1861	OE2	GLU	755	32.075	-14.728	60.719	1.00	62.46

1862	C	GLU	755	32.068	-10.912	61.252	1.00	60.75
1863	O	GLU	755	32.906	-11.809	61.240	1.00	61.42
1864	N	ILE	756	32.363	-9.677	61.636	1.00	60.43
1865	CA	ILE	756	33.709	-9.328	62.074	1.00	65.41
1866	CB	ILE	756	34.369	-8.336	61.114	1.00	58.24
1867	CG2	ILE	756	35.741	-7.964	61.623	1.00	57.70
1868	CG1	ILE	756	34.478	-8.957	59.729	1.00	59.57
1869	CD1	ILE	756	35.178	-8.090	58.743	1.00	61.24
1870	C	ILE	756	33.625	-8.693	63.439	1.00	63.18
1871	O	ILE	756	34.373	-9.043	64.351	1.00	58.77
1872	N	ILE	757	32.705	-7.740	63.548	1.00	59.89
1873	CA	ILE	757	32.434	-7.024	64.785	1.00	61.90
1874	CB	ILE	757	31.115	-6.254	64.668	1.00	64.77
1875	CG2	ILE	757	30.778	-5.602	65.991	1.00	62.61
1876	CG1	ILE	757	31.224	-5.237	63.529	1.00	62.60
1877	CD1	ILE	757	29.902	-4.649	63.097	1.00	59.02
1878	C	ILE	757	32.298	-8.069	65.879	1.00	60.76
1879	O	ILE	757	32.990	-8.016	66.890	1.00	60.98
1880	N	THR	758	31.396	-9.022	65.660	1.00	59.72
1881	CA	THR	758	31.184	-10.104	66.608	1.00	61.21
1882	CB	THR	758	30.224	-11.141	66.017	1.00	58.63
1883	OG1	THR	758	30.260	-11.028	64.592	1.00	60.88
1884	CG2	THR	758	28.792	-10.925	66.527	1.00	60.75
1885	C	THR	758	32.540	-10.770	66.885	1.00	61.53
1886	O	THR	758	33.167	-10.549	67.926	1.00	61.44
1887	N	ASN	759	32.979	-11.572	65.924	1.00	62.04
1888	CA	ASN	759	34.240	-12.305	65.965	1.00	60.58
1889	CB	ASN	759	34.426	-13.001	64.623	1.00	60.54
1890	CG	ASN	759	33.242	-12.774	63.689	1.00	60.06
1891	OD1	ASN	759	32.581	-11.723	63.736	1.00	59.27
1892	ND2	ASN	759	32.976	-13.747	62.825	1.00	59.97
1893	C	ASN	759	35.470	-11.432	66.249	1.00	59.08
1894	O	ASN	759	36.564	-11.710	65.734	1.00	63.02
1895	N	GLN	760	35.282	-10.388	67.059	1.00	60.43
1896	CA	GLN	760	36.336	-9.442	67.438	1.00	61.43
1897	CB	GLN	760	36.620	-8.446	66.302	1.00	56.98
1898	CG	GLN	760	37.445	-8.966	65.121	1.00	61.31
1899	CD	GLN	760	38.839	-9.446	65.514	1.00	63.88
1900	OE1	GLN	760	39.445	-8.949	66.463	1.00	59.43
1901	NE2	GLN	760	39.356	-10.409	64.769	1.00	62.96
1902	C	GLN	760	35.850	-8.659	68.651	1.00	59.31
1903	O	GLN	760	36.625	-8.353	69.563	1.00	59.88
1904	N	ILE	761	34.546	-8.371	68.649	1.00	61.08
1905	CA	ILE	761	33.861	-7.606	69.704	1.00	64.40
1906	CB	ILE	761	32.318	-7.582	69.469	1.00	60.77
1907	CG2	ILE	761	31.759	-8.983	69.575	1.00	61.46
1908	CG1	ILE	761	31.626	-6.686	70.500	1.00	61.86
1909	CD1	ILE	761	30.115	-6.703	70.390	1.00	62.34

1910	C	ILE	761	34.111	-8.077	71.139	1.00	63.06
1911	O	ILE	761	33.900	-7.317	72.087	1.00	60.11
1912	N	PRO	762	34.543	-9.338	71.319	1.00	58.19
1913	CD	PRO	762	34.581	-10.454	70.353	1.00	61.52
1914	CA	PRO	762	34.800	-9.840	72.670	1.00	60.05
1915	CB	PRO	762	34.718	-11.350	72.482	1.00	60.47
1916	CG	PRO	762	35.309	-11.528	71.122	1.00	62.98
1917	C	PRO	762	36.160	-9.419	73.230	1.00	59.07
1918	O	PRO	762	36.257	-8.697	74.232	1.00	61.15
1919	N	LYS	763	37.203	-9.887	72.558	1.00	59.41
1920	CA	LYS	763	38.580	-9.637	72.960	1.00	61.27
1921	CB	LYS	763	39.424	-10.882	72.594	1.00	61.66
1922	CG	LYS	763	40.926	-10.651	72.347	1.00	62.08
1923	CD	LYS	763	41.206	-9.910	71.025	1.00	58.99
1924	CE	LYS	763	40.834	-10.723	69.776	1.00	60.53
1925	NZ	LYS	763	39.378	-11.026	69.623	1.00	62.94
1926	C	LYS	763	39.256	-8.359	72.438	1.00	63.01
1927	O	LYS	763	40.164	-7.846	73.086	1.00	63.43
1928	N	TYR	764	38.820	-7.847	71.289	1.00	64.75
1929	CA	TYR	764	39.428	-6.653	70.673	1.00	58.42
1930	CB	TYR	764	38.399	-5.865	69.876	1.00	62.63
1931	CG	TYR	764	38.901	-5.590	68.486	1.00	65.16
1932	CD1	TYR	764	38.708	-6.516	67.467	1.00	57.96
1933	CE1	TYR	764	39.190	-6.287	66.180	1.00	61.30
1934	CD2	TYR	764	39.600	-4.422	68.192	1.00	61.22
1935	CE2	TYR	764	40.092	-4.183	66.902	1.00	61.36
1936	CZ	TYR	764	39.876	-5.118	65.901	1.00	59.50
1937	OH	TYR	764	40.304	-4.863	64.612	1.00	62.78
1938	C	TYR	764	40.204	-5.654	71.535	1.00	61.96
1939	O	TYR	764	41.310	-5.963	72.003	1.00	61.04
1940	N	SER	765	39.653	-4.443	71.701	1.00	60.29
1941	CA	SER	765	40.324	-3.419	72.519	1.00	61.03
1942	CB	SER	765	39.780	-1.999	72.208	1.00	57.40
1943	OG	SER	765	38.359	-1.934	72.144	1.00	59.00
1944	C	SER	765	40.207	-3.760	74.016	1.00	59.80
1945	O	SER	765	39.574	-3.046	74.809	1.00	60.59
1946	N	ASN	766	40.833	-4.884	74.371	1.00	59.36
1947	CA	ASN	766	40.867	-5.404	75.738	1.00	63.02
1948	CB	ASN	766	40.390	-6.867	75.745	1.00	59.32
1949	CG	ASN	766	38.959	-7.018	75.239	1.00	61.45
1950	OD1	ASN	766	38.593	-6.456	74.197	1.00	60.60
1951	ND2	ASN	766	38.143	-7.782	75.971	1.00	64.82
1952	C	ASN	766	42.301	-5.305	76.311	1.00	62.76
1953	O	ASN	766	42.503	-4.889	77.469	1.00	60.59
1954	N	GLY	767	43.281	-5.673	75.478	1.00	59.11
1955	CA	GLY	767	44.689	-5.653	75.860	1.00	59.91
1956	C	GLY	767	45.366	-6.867	75.232	1.00	61.75
1957	O	GLY	767	46.588	-6.912	75.041	1.00	61.17

1958	N	ASN	768	44.532	-7.846	74.887	1.00	62.80
1959	CA	ASN	768	44.942	-9.109	74.276	1.00	62.46
1960	CB	ASN	768	43.717	-10.032	74.246	1.00	59.72
1961	CG	ASN	768	42.798	-9.832	75.467	1.00	60.42
1962	OD1	ASN	768	41.697	-10.404	75.538	1.00	59.89
1963	ND2	ASN	768	43.248	-9.020	76.427	1.00	63.45
1964	C	ASN	768	45.543	-8.940	72.855	1.00	63.10
1965	O	ASN	768	46.095	-9.882	72.282	1.00	62.80
1966	N	ILE	769	45.418	-7.744	72.284	1.00	58.10
1967	CA	ILE	769	45.984	-7.464	70.967	1.00	60.18
1968	CB	ILE	769	45.006	-6.713	70.036	1.00	61.64
1969	CG2	ILE	769	45.569	-6.703	68.614	1.00	59.97
1970	CG1	ILE	769	43.623	-7.361	70.051	1.00	65.54
1971	CD1	ILE	769	42.605	-6.626	69.175	1.00	65.14
1972	C	ILE	769	47.192	-6.544	71.150	1.00	59.44
1973	O	ILE	769	47.217	-5.701	72.058	1.00	61.97
1974	N	LYS	770	48.175	-6.692	70.267	1.00	61.57
1975	CA	LYS	770	49.391	-5.890	70.314	1.00	60.09
1976	CB	LYS	770	50.601	-6.778	70.033	1.00	61.51
1977	CG	LYS	770	51.961	-6.172	70.339	1.00	61.08
1978	CD	LYS	770	53.041	-7.224	70.047	1.00	59.40
1979	CE	LYS	770	54.344	-6.982	70.801	1.00	62.15
1980	NZ	LYS	770	55.339	-8.089	70.604	1.00	63.19
1981	C	LYS	770	49.333	-4.776	69.277	1.00	63.90
1982	O	LYS	770	49.439	-5.031	68.071	1.00	62.08
1983	N	LYS	771	49.161	-3.545	69.754	1.00	59.06
1984	CA	LYS	771	49.103	-2.376	68.884	1.00	61.08
1985	CB	LYS	771	48.386	-1.212	69.589	1.00	63.15
1986	CG	LYS	771	49.188	-0.525	70.712	1.00	63.84
1987	CD	LYS	771	48.443	0.681	71.308	1.00	63.12
1988	CE	LYS	771	49.384	1.588	72.100	1.00	59.83
1989	NZ	LYS	771	48.821	2.970	72.186	1.00	60.16
1990	C	LYS	771	50.532	-1.976	68.550	1.00	60.42
1991	O	LYS	771	51.276	-1.561	69.430	1.00	62.03
1992	N	LEU	772	50.928	-2.120	67.290	1.00	60.80
1993	CA	LEU	772	52.285	-1.756	66.890	1.00	58.97
1994	CB	LEU	772	52.629	-2.368	65.533	1.00	62.77
1995	CG	LEU	772	52.781	-3.885	65.492	1.00	63.82
1996	CD1	LEU	772	52.780	-4.346	64.046	1.00	62.61
1997	CD2	LEU	772	54.071	-4.295	66.203	1.00	63.11
1998	C	LEU	772	52.405	-0.243	66.812	1.00	61.57
1999	O	LEU	772	51.513	0.428	66.289	1.00	60.62
2000	N	LEU	773	53.499	0.296	67.341	1.00	59.76
2001	CA	LEU	773	53.704	1.734	67.317	1.00	60.00
2002	CB	LEU	773	53.602	2.320	68.725	1.00	59.66
2003	CG	LEU	773	52.221	2.321	69.380	1.00	62.80
2004	CD1	LEU	773	52.290	2.999	70.729	1.00	61.23
2005	CD2	LEU	773	51.233	3.053	68.490	1.00	65.68

2006	C	LEU	773	55.051	2.094	66.727	1.00	62.80
2007	O	LEU	773	55.911	1.234	66.517	1.00	61.81
2008	N	PHE	774	55.219	3.382	66.456	1.00	60.94
2009	CA	PHE	774	56.451	3.917	65.897	1.00	61.49
2010	CB	PHE	774	56.128	4.864	64.743	1.00	63.45
2011	CG	PHE	774	55.889	4.169	63.451	1.00	61.20
2012	CD1	PHE	774	56.936	3.532	62.802	1.00	63.76
2013	CD2	PHE	774	54.621	4.105	62.902	1.00	61.89
2014	CE1	PHE	774	56.727	2.838	61.627	1.00	56.93
2015	CE2	PHE	774	54.395	3.409	61.720	1.00	59.92
2016	CZ	PHE	774	55.451	2.773	61.081	1.00	62.56
2017	C	PHE	774	57.175	4.681	66.984	1.00	60.20
2018	O	PHE	774	58.400	4.702	67.046	1.00	60.03
2019	N	HIS	775	56.384	5.301	67.849	1.00	62.48
2020	CA	HIS	775	56.905	6.104	68.934	1.00	64.64
2021	CB	HIS	775	56.466	7.558	68.730	1.00	61.69
2022	CG	HIS	775	56.898	8.120	67.417	1.00	59.70
2023	CD2	HIS	775	56.188	8.565	66.356	1.00	62.49
2024	ND1	HIS	775	58.223	8.191	67.047	1.00	60.30
2025	CE1	HIS	775	58.313	8.652	65.813	1.00	59.19
2026	NE2	HIS	775	57.092	8.886	65.370	1.00	59.04
2027	C	HIS	775	56.428	5.596	70.277	1.00	64.58
2028	O	HIS	775	55.390	4.948	70.373	1.00	58.66
2029	N	GLN	776	57.203	5.895	71.311	1.00	60.50
2030	CA	GLN	776	56.864	5.502	72.669	1.00	61.43
2031	CB	GLN	776	58.154	5.293	73.457	1.00	59.86
2032	CG	GLN	776	59.281	6.243	73.042	1.00	57.49
2033	CD	GLN	776	60.679	5.638	73.241	1.00	60.53
2034	OE1	GLN	776	61.696	6.265	72.919	1.00	61.97
2035	NE2	GLN	776	60.730	4.412	73.772	1.00	60.63
2036	C	GLN	776	55.993	6.583	73.335	1.00	60.06
2037	O	GLN	776	56.098	7.765	72.919	1.00	61.84
2038	OXT	GLN	776	55.219	6.239	74.268	1.00	60.74
2039	CB	GLU	741	35.922	-16.424	65.488	1.00	58.89
2040	CG	GLU	741	36.766	-17.078	64.386	1.00	67.76
2041	CD	GLU	741	38.144	-16.463	64.277	1.00	60.66
2042	OE1	GLU	741	38.838	-16.698	63.252	1.00	59.66
2043	OE2	GLU	741	38.524	-15.741	65.233	1.00	61.27
2044	C	GLU	741	33.996	-16.854	64.024	1.00	61.38
2045	O	GLU	741	33.681	-15.808	63.464	1.00	63.70
2046	N	GLU	741	34.336	-18.280	65.946	1.00	62.41
2047	CA	GLU	741	34.460	-16.870	65.464	1.00	59.35
2048	N	GLU	742	33.995	-18.034	63.422	1.00	58.35
2049	CA	GLU	742	33.594	-18.184	62.036	1.00	63.61
2050	CB	GLU	742	32.158	-17.672	61.824	1.00	60.80
2051	CG	GLU	742	31.516	-18.155	60.518	1.00	62.06
2052	CD	GLU	742	31.783	-19.645	60.238	1.00	63.64
2053	OE1	GLU	742	31.146	-20.190	59.309	1.00	64.92

2054	OE2	GLU	742	32.632	-20.276	60.925	1.00	62.96
2055	C	GLU	742	34.541	-17.482	61.064	1.00	61.07
2056	O	GLU	742	35.655	-17.950	60.825	1.00	59.51
2057	N	ASN	743	34.090	-16.355	60.522	1.00	61.83
2058	CA	ASN	743	34.850	-15.586	59.535	1.00	60.95
2059	CB	ASN	743	36.300	-15.368	59.987	1.00	61.82
2060	CG	ASN	743	36.418	-14.360	61.118	1.00	64.29
2061	OD1	ASN	743	36.646	-14.729	62.277	1.00	58.19
2062	ND2	ASN	743	36.262	-13.077	60.787	1.00	58.54
2063	C	ASN	743	34.842	-16.318	58.192	1.00	60.80
2064	O	ASN	743	35.780	-16.196	57.410	1.00	62.67
2065	N	ALA	744	33.779	-17.075	57.935	1.00	59.69
2066	CA	ALA	744	33.640	-17.827	56.696	1.00	61.76
2067	CB	ALA	744	32.350	-18.623	56.729	1.00	60.04
2068	C	ALA	744	33.675	-16.930	55.453	1.00	62.63
2069	O	ALA	744	34.423	-17.199	54.503	1.00	58.54
2070	N	LEU	745	32.869	-15.866	55.462	1.00	60.19
2071	CA	LEU	745	32.820	-14.936	54.329	1.00	62.12
2072	CB	LEU	745	31.855	-13.783	54.617	1.00	60.59
2073	CG	LEU	745	30.606	-13.726	53.739	1.00	58.63
2074	CD1	LEU	745	29.895	-12.400	53.937	1.00	64.25
2075	CD2	LEU	745	31.004	-13.902	52.291	1.00	60.41
2076	C	LEU	745	34.190	-14.360	53.952	1.00	61.72
2077	O	LEU	745	34.521	-14.276	52.776	1.00	59.83
2078	N	LEU	746	34.978	-13.961	54.946	1.00	57.79
2079	CA	LEU	746	36.311	-13.413	54.691	1.00	60.45
2080	CB	LEU	746	36.898	-12.849	55.989	1.00	61.06
2081	CG	LEU	746	37.673	-11.534	55.956	1.00	61.13
2082	CD1	LEU	746	38.380	-11.374	57.275	1.00	61.70
2083	CD2	LEU	746	38.664	-11.520	54.823	1.00	61.56
2084	C	LEU	746	37.249	-14.511	54.156	1.00	58.73
2085	O	LEU	746	37.905	-14.356	53.120	1.00	62.68
2086	N	ARG	747	37.307	-15.613	54.895	1.00	61.00
2087	CA	ARG	747	38.145	-16.759	54.560	1.00	57.24
2088	CB	ARG	747	37.853	-17.906	55.539	1.00	66.74
2089	CG	ARG	747	38.332	-19.278	55.102	1.00	61.05
2090	CD	ARG	747	38.533	-20.190	56.319	1.00	62.51
2091	NE	ARG	747	39.807	-19.938	56.998	1.00	62.06
2092	CZ	ARG	747	39.952	-19.867	58.321	1.00	63.78
2093	NH1	ARG	747	38.894	-20.023	59.118	1.00	60.31
2094	NH2	ARG	747	41.156	-19.637	58.848	1.00	60.80
2095	C	ARG	747	37.883	-17.186	53.134	1.00	59.12
2096	O	ARG	747	38.793	-17.589	52.418	1.00	62.02
2097	N	TYR	748	36.623	-17.088	52.731	1.00	61.89
2098	CA	TYR	748	36.215	-17.449	51.387	1.00	65.00
2099	CB	TYR	748	34.685	-17.413	51.301	1.00	58.95
2100	CG	TYR	748	34.136	-17.350	49.897	1.00	62.12
2101	CD1	TYR	748	34.256	-18.429	49.021	1.00	63.79

2102	CE1	TYR	748	33.805	-18.342	47.715	1.00	61.69
2103	CD2	TYR	748	33.544	-16.185	49.430	1.00	61.63
2104	CE2	TYR	748	33.091	-16.084	48.127	1.00	60.08
2105	CZ	TYR	748	33.226	-17.163	47.272	1.00	58.42
2106	OH	TYR	748	32.806	-17.030	45.966	1.00	59.74
2107	C	TYR	748	36.832	-16.447	50.419	1.00	61.75
2108	O	TYR	748	37.599	-16.807	49.532	1.00	61.82
2109	N	LEU	749	36.501	-15.178	50.628	1.00	60.52
2110	CA	LEU	749	36.974	-14.069	49.800	1.00	61.53
2111	CB	LEU	749	36.380	-12.757	50.303	1.00	63.00
2112	CG	LEU	749	34.873	-12.741	50.535	1.00	57.09
2113	CD1	LEU	749	34.508	-11.427	51.167	1.00	62.85
2114	CD2	LEU	749	34.113	-12.954	49.233	1.00	62.37
2115	C	LEU	749	38.482	-13.910	49.733	1.00	64.05
2116	O	LEU	749	38.991	-13.275	48.807	1.00	61.97
2117	N	LEU	750	39.195	-14.475	50.703	1.00	59.99
2118	CA	LEU	750	40.644	-14.363	50.728	1.00	63.11
2119	CB	LEU	750	41.147	-14.497	52.167	1.00	62.65
2120	CG	LEU	750	41.463	-13.160	52.849	1.00	63.02
2121	CD1	LEU	750	41.695	-13.344	54.327	1.00	58.04
2122	CD2	LEU	750	42.693	-12.559	52.194	1.00	62.24
2123	C	LEU	750	41.436	-15.294	49.803	1.00	64.30
2124	O	LEU	750	42.666	-15.246	49.796	1.00	58.24
2125	N	ASP	751	40.745	-16.129	49.024	1.00	59.30
2126	CA	ASP	751	41.396	-17.048	48.068	1.00	62.49
2127	CB	ASP	751	41.860	-18.337	48.764	1.00	62.90
2128	CG	ASP	751	40.921	-18.784	49.855	1.00	62.09
2129	OD1	ASP	751	40.342	-17.900	50.526	1.00	62.68
2130	OD2	ASP	751	40.779	-20.014	50.051	1.00	60.33
2131	C	ASP	751	40.472	-17.371	46.897	1.00	61.25
2132	O	ASP	751	39.476	-18.065	47.053	1.00	61.96
2133	N	LYS	752	40.824	-16.849	45.725	1.00	62.34
2134	CA	LYS	752	40.030	-17.003	44.506	1.00	62.50
2135	CB	LYS	752	38.733	-16.160	44.600	1.00	63.17
2136	CG	LYS	752	37.872	-16.386	45.858	1.00	60.82
2137	CD	LYS	752	36.923	-15.230	46.159	1.00	62.16
2138	CE	LYS	752	35.726	-15.186	45.223	1.00	60.30
2139	NZ	LYS	752	36.101	-15.095	43.779	1.00	61.47
2140	C	LYS	752	40.895	-16.438	43.384	1.00	63.98
2141	O	LYS	752	42.043	-16.833	43.212	1.00	60.08
2142	N	ASP	753	40.322	-15.496	42.641	1.00	61.50
2143	CA	ASP	753	41.004	-14.809	41.552	1.00	60.87
2144	CB	ASP	753	41.969	-13.778	42.151	1.00	61.81
2145	CG	ASP	753	41.293	-12.886	43.212	1.00	65.36
2146	OD1	ASP	753	40.845	-13.417	44.262	1.00	58.98
2147	OD2	ASP	753	41.204	-11.653	42.996	1.00	62.40
2148	C	ASP	753	41.712	-15.723	40.533	1.00	62.25
2149	O	ASP	753	41.905	-16.929	40.770	1.00	62.51

2150	N	ASP	754	42.076	-15.125	39.394	1.00	59.26
2151	CA	ASP	754	42.713	-15.818	38.271	1.00	62.08
2152	CB	ASP	754	42.118	-15.302	36.949	1.00	60.51
2153	CG	ASP	754	41.121	-14.148	37.150	1.00	60.95
2154	OD1	ASP	754	40.683	-13.555	36.135	1.00	61.57
2155	OD2	ASP	754	40.762	-13.831	38.304	1.00	61.61
2156	C	ASP	754	44.236	-15.678	38.234	1.00	60.21
2157	O	ASP	754	44.946	-16.712	38.264	1.00	63.29
2158	OXT	ASP	754	44.707	-14.526	38.169	1.00	61.39
2159	CB	GLN	527	44.425	43.308	57.458	1.00	59.84
2160	CG	GLN	527	45.330	43.181	58.697	1.00	63.06
2161	CD	GLN	527	46.173	41.895	58.675	1.00	61.64
2162	OE1	GLN	527	46.913	41.596	59.623	1.00	62.44
2163	NE2	GLN	527	46.065	41.137	57.583	1.00	63.46
2164	C	GLN	527	43.994	44.763	55.475	1.00	60.61
2165	O	GLN	527	44.711	45.517	54.798	1.00	61.62
2166	N	GLN	527	42.843	45.238	57.671	1.00	62.80
2167	CA	GLN	527	44.095	44.745	57.006	1.00	60.11
2168	N	LEU	528	43.105	43.912	54.955	1.00	62.93
2169	CA	LEU	528	42.857	43.747	53.516	1.00	58.92
2170	CB	LEU	528	43.696	42.579	52.979	1.00	61.24
2171	CG	LEU	528	45.210	42.751	53.124	1.00	58.97
2172	CD1	LEU	528	45.858	41.410	53.501	1.00	57.95
2173	CD2	LEU	528	45.778	43.371	51.831	1.00	60.61
2174	C	LEU	528	41.369	43.449	53.303	1.00	63.94
2175	O	LEU	528	40.531	44.290	53.650	1.00	62.36
2176	N	THR	529	41.067	42.256	52.748	1.00	59.95
2177	CA	THR	529	39.689	41.769	52.487	1.00	61.84
2178	CB	THR	529	39.396	40.430	53.232	1.00	59.05
2179	OG1	THR	529	40.375	39.442	52.866	1.00	63.83
2180	CG2	THR	529	37.997	39.920	52.882	1.00	59.80
2181	C	THR	529	38.725	42.842	52.992	1.00	61.32
2182	O	THR	529	37.988	42.645	53.973	1.00	61.35
2183	N	PRO	530	38.704	43.977	52.271	1.00	64.25
2184	CD	PRO	530	38.650	43.494	50.878	1.00	59.35
2185	CA	PRO	530	38.021	45.276	52.317	1.00	58.74
2186	CB	PRO	530	37.610	45.502	50.860	1.00	60.27
2187	CG	PRO	530	37.368	44.132	50.384	1.00	65.84
2188	C	PRO	530	36.839	45.387	53.239	1.00	62.92
2189	O	PRO	530	36.948	45.328	54.474	1.00	60.28
2190	N	THR	531	35.706	45.591	52.590	1.00	63.85
2191	CA	THR	531	34.443	45.708	53.246	1.00	62.34
2192	CB	THR	531	34.253	47.135	53.851	1.00	63.80
2193	OG1	THR	531	33.854	47.016	55.230	1.00	64.25
2194	CG2	THR	531	33.218	47.940	53.067	1.00	61.34
2195	C	THR	531	33.526	45.410	52.081	1.00	61.78
2196	O	THR	531	32.505	44.758	52.251	1.00	61.93
2197	N	LEU	532	33.917	45.822	50.877	1.00	62.02

2198	CA	LEU	532	33.060	45.545	49.722	1.00	60.94
2199	CB	LEU	532	33.410	46.445	48.528	1.00	57.32
2200	CG	LEU	532	32.463	46.285	47.329	1.00	64.49
2201	CD1	LEU	532	31.027	46.313	47.771	1.00	61.90
2202	CD2	LEU	532	32.702	47.377	46.344	1.00	62.84
2203	C	LEU	532	33.077	44.077	49.283	1.00	61.37
2204	O	LEU	532	32.016	43.461	49.149	1.00	62.65
2205	N	VAL	533	34.266	43.518	49.052	1.00	61.22
2206	CA	VAL	533	34.366	42.119	48.635	1.00	60.75
2207	CB	VAL	533	35.781	41.753	48.114	1.00	59.58
2208	CG1	VAL	533	36.697	41.400	49.264	1.00	60.31
2209	CG2	VAL	533	35.695	40.576	47.185	1.00	59.77
2210	C	VAL	533	34.062	41.240	49.840	1.00	63.61
2211	O	VAL	533	33.861	40.038	49.709	1.00	62.93
2212	N	SER	534	34.053	41.859	51.013	1.00	61.64
2213	CA	SER	534	33.774	41.170	52.260	1.00	60.61
2214	CB	SER	534	34.143	42.089	53.425	1.00	62.32
2215	OG	SER	534	34.391	41.364	54.612	1.00	60.70
2216	C	SER	534	32.276	40.880	52.270	1.00	62.67
2217	O	SER	534	31.799	39.906	52.854	1.00	59.90
2218	N	LEU	535	31.544	41.747	51.593	1.00	60.18
2219	CA	LEU	535	30.102	41.644	51.508	1.00	60.75
2220	CB	LEU	535	29.527	42.975	51.048	1.00	61.59
2221	CG	LEU	535	28.027	43.101	51.245	1.00	61.16
2222	CD1	LEU	535	27.773	43.835	52.537	1.00	63.92
2223	CD2	LEU	535	27.416	43.850	50.089	1.00	61.72
2224	C	LEU	535	29.688	40.547	50.543	1.00	60.18
2225	O	LEU	535	28.852	39.714	50.868	1.00	58.39
2226	N	LEU	536	30.269	40.552	49.349	1.00	60.57
2227	CA	LEU	536	29.950	39.536	48.355	1.00	63.14
2228	CB	LEU	536	30.813	39.719	47.115	1.00	61.69
2229	CG	LEU	536	30.671	40.980	46.284	1.00	63.99
2230	CD1	LEU	536	31.622	40.864	45.118	1.00	60.60
2231	CD2	LEU	536	29.247	41.145	45.801	1.00	62.81
2232	C	LEU	536	30.204	38.140	48.908	1.00	61.72
2233	O	LEU	536	29.703	37.141	48.379	1.00	60.04
2234	N	GLU	537	30.996	38.086	49.970	1.00	60.48
2235	CA	GLU	537	31.359	36.838	50.607	1.00	61.60
2236	CB	GLU	537	32.691	37.003	51.307	1.00	61.56
2237	CG	GLU	537	33.169	35.763	51.998	1.00	58.70
2238	CD	GLU	537	34.599	35.907	52.442	1.00	62.52
2239	OE1	GLU	537	35.173	34.900	52.919	1.00	61.18
2240	OE2	GLU	537	35.140	37.033	52.305	1.00	60.21
2241	C	GLU	537	30.344	36.288	51.592	1.00	59.30
2242	O	GLU	537	30.094	35.084	51.604	1.00	60.22
2243	N	VAL	538	29.773	37.155	52.424	1.00	61.88
2244	CA	VAL	538	28.781	36.714	53.399	1.00	62.81
2245	CB	VAL	538	28.636	37.687	54.591	1.00	57.08

2246	CG1	VAL	538	29.993	38.283	54.957	1.00	61.43
2247	CG2	VAL	538	27.611	38.757	54.268	1.00	60.61
2248	C	VAL	538	27.420	36.586	52.752	1.00	61.99
2249	O	VAL	538	26.576	35.841	53.233	1.00	61.89
2250	N	ILE	539	27.203	37.322	51.669	1.00	61.34
2251	CA	ILE	539	25.931	37.263	50.977	1.00	60.88
2252	CB	ILE	539	25.628	38.548	50.209	1.00	57.53
2253	CG2	ILE	539	26.034	39.737	51.035	1.00	63.74
2254	CG1	ILE	539	26.365	38.550	48.869	1.00	64.95
2255	CD1	ILE	539	25.847	39.584	47.898	1.00	61.40
2256	C	ILE	539	25.946	36.133	49.977	1.00	59.86
2257	O	ILE	539	24.984	35.934	49.251	1.00	60.95
2258	N	GLU	540	27.051	35.408	49.919	1.00	61.19
2259	CA	GLU	540	27.170	34.290	48.993	1.00	64.61
2260	CB	GLU	540	28.620	33.798	48.960	1.00	61.89
2261	CG	GLU	540	28.917	32.628	48.022	1.00	59.99
2262	CD	GLU	540	28.635	32.926	46.560	1.00	60.98
2263	OE1	GLU	540	28.949	34.050	46.103	1.00	60.19
2264	OE2	GLU	540	28.113	32.025	45.861	1.00	58.09
2265	C	GLU	540	26.241	33.181	49.469	1.00	60.25
2266	O	GLU	540	26.357	32.710	50.603	1.00	62.79
2267	N	PRO	541	25.289	32.766	48.614	1.00	59.70
2268	CD	PRO	541	24.961	33.287	47.275	1.00	61.01
2269	CA	PRO	541	24.362	31.703	49.013	1.00	61.09
2270	CB	PRO	541	23.361	31.665	47.861	1.00	63.13
2271	CG	PRO	541	24.138	32.177	46.694	1.00	57.00
2272	C	PRO	541	25.051	30.365	49.254	1.00	60.83
2273	O	PRO	541	25.979	29.988	48.535	1.00	60.28
2274	N	GLU	542	24.607	29.669	50.297	1.00	60.82
2275	CA	GLU	542	25.157	28.364	50.655	1.00	61.11
2276	CB	GLU	542	24.607	27.933	52.001	1.00	63.94
2277	CG	GLU	542	23.163	27.558	51.899	1.00	65.51
2278	CD	GLU	542	22.569	27.217	53.237	1.00	61.20
2279	OE1	GLU	542	21.369	26.813	53.269	1.00	64.82
2280	OE2	GLU	542	23.307	27.360	54.253	1.00	61.05
2281	C	GLU	542	24.668	27.393	49.584	1.00	60.85
2282	O	GLU	542	23.631	27.637	48.966	1.00	61.52
2283	N	VAL	543	25.369	26.291	49.353	1.00	62.89
2284	CA	VAL	543	24.879	25.397	48.316	1.00	61.20
2285	CB	VAL	543	26.029	24.589	47.676	1.00	60.15
2286	CG1	VAL	543	27.366	25.164	48.116	1.00	61.25
2287	CG2	VAL	543	25.903	23.132	48.011	1.00	64.25
2288	C	VAL	543	23.745	24.465	48.760	1.00	61.19
2289	O	VAL	543	23.506	24.232	49.955	1.00	61.59
2290	N	LEU	544	23.037	23.944	47.769	1.00	60.75
2291	CA	LEU	544	21.910	23.068	48.018	1.00	62.70
2292	CB	LEU	544	20.686	23.557	47.244	1.00	61.76
2293	CG	LEU	544	20.315	25.041	47.237	1.00	62.21

2294	CD1	LEU	544	19.968	25.490	48.639	1.00	60.39
2295	CD2	LEU	544	21.464	25.856	46.654	1.00	61.37
2296	C	LEU	544	22.209	21.639	47.591	1.00	61.62
2297	O	LEU	544	23.047	21.388	46.721	1.00	61.82
2298	N	TYR	545	21.504	20.713	48.222	1.00	60.41
2299	CA	TYR	545	21.623	19.306	47.915	1.00	64.14
2300	CB	TYR	545	21.436	18.495	49.189	1.00	59.96
2301	CG	TYR	545	22.566	18.713	50.160	1.00	66.69
2302	CD1	TYR	545	22.715	17.908	51.287	1.00	63.31
2303	CE1	TYR	545	23.810	18.056	52.122	1.00	61.54
2304	CD2	TYR	545	23.537	19.684	49.907	1.00	62.21
2305	CE2	TYR	545	24.632	19.843	50.739	1.00	61.49
2306	CZ	TYR	545	24.769	19.022	51.842	1.00	59.50
2307	OH	TYR	545	25.898	19.142	52.619	1.00	60.93
2308	C	TYR	545	20.482	19.111	46.949	1.00	58.64
2309	O	TYR	545	19.553	19.912	46.956	1.00	62.56
2310	N	ALA	546	20.532	18.077	46.115	1.00	57.51
2311	CA	ALA	546	19.461	17.886	45.145	1.00	59.14
2312	CB	ALA	546	20.026	17.390	43.845	1.00	60.50
2313	C	ALA	546	18.347	16.965	45.595	1.00	62.16
2314	O	ALA	546	17.352	16.821	44.895	1.00	62.38
2315	N	GLY	547	18.493	16.338	46.755	1.00	59.60
2316	CA	GLY	547	17.441	15.445	47.203	1.00	63.46
2317	C	GLY	547	17.125	14.408	46.137	1.00	63.02
2318	O	GLY	547	15.968	14.068	45.890	1.00	60.60
2319	N	TYR	548	18.180	13.918	45.496	1.00	62.10
2320	CA	TYR	548	18.095	12.906	44.447	1.00	60.16
2321	CB	TYR	548	19.366	12.971	43.621	1.00	60.58
2322	CG	TYR	548	19.357	12.107	42.403	1.00	61.55
2323	CD1	TYR	548	18.522	12.406	41.331	1.00	65.33
2324	CE1	TYR	548	18.550	11.657	40.175	1.00	62.35
2325	CD2	TYR	548	20.218	11.023	42.292	1.00	62.44
2326	CE2	TYR	548	20.251	10.267	41.142	1.00	64.59
2327	CZ	TYR	548	19.416	10.594	40.086	1.00	60.42
2328	OH	TYR	548	19.467	9.877	38.925	1.00	60.60
2329	C	TYR	548	17.979	11.519	45.080	1.00	60.53
2330	O	TYR	548	18.584	11.272	46.114	1.00	61.95
2331	N	ASP	549	17.227	10.603	44.480	1.00	60.31
2332	CA	ASP	549	17.135	9.281	45.088	1.00	60.89
2333	CB	ASP	549	16.206	8.359	44.317	1.00	61.64
2334	CG	ASP	549	15.653	7.256	45.196	1.00	62.87
2335	OD1	ASP	549	16.437	6.715	45.997	1.00	61.92
2336	OD2	ASP	549	14.446	6.929	45.100	1.00	58.12
2337	C	ASP	549	18.525	8.656	45.152	1.00	62.05
2338	O	ASP	549	19.176	8.728	46.190	1.00	59.43
2339	N	SER	550	18.977	8.052	44.049	1.00	61.36
2340	CA	SER	550	20.312	7.425	43.963	1.00	61.16
2341	CB	SER	550	21.301	8.127	44.910	1.00	61.33

2342	OG	SER	550	22.637	8.055	44.435	1.00	65.58
2343	C	SER	550	20.286	5.923	44.268	1.00	62.72
2344	O	SER	550	21.025	5.138	43.662	1.00	61.37
2345	N	SER	551	19.422	5.543	45.206	1.00	60.55
2346	CA	SER	551	19.262	4.155	45.623	1.00	62.47
2347	CB	SER	551	18.461	4.092	46.927	1.00	59.78
2348	OG	SER	551	17.138	4.551	46.727	1.00	65.75
2349	C	SER	551	18.548	3.348	44.544	1.00	61.26
2350	O	SER	551	18.187	2.189	44.749	1.00	64.05
2351	N	VAL	552	18.349	3.976	43.394	1.00	61.88
2352	CA	VAL	552	17.683	3.338	42.268	1.00	61.07
2353	CB	VAL	552	16.146	3.536	42.346	1.00	61.01
2354	CG1	VAL	552	15.781	4.362	43.582	1.00	62.13
2355	CG2	VAL	552	15.642	4.194	41.084	1.00	63.59
2356	C	VAL	552	18.245	3.935	40.975	1.00	60.74
2357	O	VAL	552	18.423	5.151	40.872	1.00	60.94
2358	N	PRO	553	18.502	3.085	39.966	1.00	57.88
2359	CD	PRO	553	17.755	1.824	39.869	1.00	60.27
2360	CA	PRO	553	19.058	3.418	38.648	1.00	60.29
2361	CB	PRO	553	18.407	2.387	37.718	1.00	59.38
2362	CG	PRO	553	17.208	1.918	38.478	1.00	59.68
2363	C	PRO	553	18.933	4.837	38.105	1.00	61.75
2364	O	PRO	553	17.864	5.452	38.132	1.00	60.81
2365	N	ASP	554	20.055	5.352	37.616	1.00	59.48
2366	CA	ASP	554	20.061	6.676	37.032	1.00	59.15
2367	CB	ASP	554	21.477	7.212	36.819	1.00	62.17
2368	CG	ASP	554	22.222	7.452	38.101	1.00	62.93
2369	OD1	ASP	554	21.591	7.655	39.164	1.00	60.70
2370	OD2	ASP	554	23.467	7.455	38.017	1.00	60.19
2371	C	ASP	554	19.433	6.505	35.667	1.00	61.49
2372	O	ASP	554	18.898	5.446	35.354	1.00	59.51
2373	N	SER	555	19.536	7.557	34.859	1.00	60.31
2374	CA	SER	555	19.023	7.601	33.492	1.00	60.74
2375	CB	SER	555	17.576	7.113	33.419	1.00	64.15
2376	OG	SER	555	16.687	8.099	33.896	1.00	60.71
2377	C	SER	555	19.092	9.069	33.108	1.00	61.31
2378	O	SER	555	18.776	9.929	33.927	1.00	59.93
2379	N	THR	556	19.525	9.358	31.883	1.00	62.16
2380	CA	THR	556	19.636	10.742	31.434	1.00	61.52
2381	CB	THR	556	19.673	10.857	29.895	1.00	59.01
2382	OG1	THR	556	20.850	10.212	29.391	1.00	60.60
2383	CG2	THR	556	19.677	12.330	29.475	1.00	60.87
2384	C	THR	556	18.422	11.505	31.913	1.00	61.95
2385	O	THR	556	18.517	12.377	32.788	1.00	60.46
2386	N	TRP	557	17.285	11.145	31.318	1.00	60.92
2387	CA	TRP	557	15.986	11.734	31.611	1.00	63.76
2388	CB	TRP	557	14.864	10.739	31.251	1.00	61.57
2389	CG	TRP	557	13.719	10.807	32.225	1.00	57.77

2390	CD2	TRP	557	12.895	11.949	32.491	1.00	60.28
2391	CE2	TRP	557	12.066	11.627	33.595	1.00	61.10
2392	CE3	TRP	557	12.785	13.219	31.911	1.00	57.69
2393	CD1	TRP	557	13.357	9.855	33.145	1.00	63.49
2394	NE1	TRP	557	12.369	10.344	33.974	1.00	60.45
2395	CZ2	TRP	557	11.132	12.535	34.132	1.00	61.64
2396	CZ3	TRP	557	11.857	14.124	32.452	1.00	61.15
2397	CH2	TRP	557	11.045	13.773	33.548	1.00	61.06
2398	C	TRP	557	15.816	12.176	33.063	1.00	61.03
2399	O	TRP	557	15.546	13.342	33.335	1.00	63.66
2400	N	ARG	558	15.972	11.228	33.982	1.00	62.37
2401	CA	ARG	558	15.798	11.466	35.413	1.00	63.98
2402	CB	ARG	558	15.806	10.116	36.134	1.00	61.30
2403	CG	ARG	558	15.389	10.127	37.590	1.00	62.22
2404	CD	ARG	558	15.189	8.686	38.070	1.00	59.18
2405	NE	ARG	558	16.210	8.204	39.005	1.00	60.75
2406	CZ	ARG	558	16.280	8.542	40.294	1.00	62.74
2407	NH1	ARG	558	15.392	9.378	40.820	1.00	65.45
2408	NH2	ARG	558	17.222	8.022	41.074	1.00	61.39
2409	C	ARG	558	16.814	12.416	36.056	1.00	63.08
2410	O	ARG	558	16.524	13.027	37.085	1.00	62.80
2411	N	ILE	559	17.991	12.548	35.451	1.00	63.40
2412	CA	ILE	559	19.036	13.423	35.983	1.00	59.67
2413	CB	ILE	559	20.459	12.828	35.701	1.00	59.65
2414	CG2	ILE	559	21.437	13.905	35.250	1.00	56.03
2415	CG1	ILE	559	20.982	12.150	36.968	1.00	58.33
2416	CD1	ILE	559	22.212	11.327	36.744	1.00	61.31
2417	C	ILE	559	18.939	14.862	35.469	1.00	64.14
2418	O	ILE	559	18.843	15.792	36.281	1.00	63.80
2419	N	MET	560	18.964	15.060	34.151	1.00	58.15
2420	CA	MET	560	18.871	16.419	33.646	1.00	61.08
2421	CB	MET	560	18.753	16.460	32.095	1.00	60.65
2422	CG	MET	560	20.117	16.352	31.322	1.00	63.74
2423	SD	MET	560	20.038	16.357	29.422	1.00	63.49
2424	CE	MET	560	21.750	16.939	28.970	1.00	61.12
2425	C	MET	560	17.634	17.014	34.325	1.00	63.02
2426	O	MET	560	17.666	18.156	34.780	1.00	60.37
2427	N	THR	561	16.572	16.217	34.457	1.00	60.33
2428	CA	THR	561	15.351	16.677	35.123	1.00	60.71
2429	CB	THR	561	14.306	15.540	35.292	1.00	58.90
2430	OG1	THR	561	14.006	14.959	34.025	1.00	60.27
2431	CG2	THR	561	13.019	16.080	35.867	1.00	58.67
2432	C	THR	561	15.616	17.259	36.520	1.00	60.71
2433	O	THR	561	15.390	18.429	36.747	1.00	62.74
2434	N	THR	562	16.111	16.434	37.451	1.00	61.67
2435	CA	THR	562	16.387	16.821	38.860	1.00	62.60
2436	CB	THR	562	16.914	15.721	39.677	1.00	60.58
2437	OG1	THR	562	18.152	15.292	39.081	1.00	59.96

2438	CG2	THR	562	15.938	14.616	39.802	1.00	62.71
2439	C	THR	562	17.487	17.786	39.098	1.00	60.58
2440	O	THR	562	17.924	18.032	40.229	1.00	63.25
2441	N	LEU	563	17.993	18.325	38.047	1.00	60.71
2442	CA	LEU	563	19.148	19.110	38.123	1.00	61.15
2443	CB	LEU	563	20.009	18.485	37.164	1.00	61.40
2444	CG	LEU	563	21.445	18.268	37.247	1.00	60.76
2445	CD1	LEU	563	21.882	17.094	38.118	1.00	59.56
2446	CD2	LEU	563	21.705	18.012	35.810	1.00	62.29
2447	C	LEU	563	18.542	20.350	37.631	1.00	60.18
2448	O	LEU	563	19.115	21.393	37.453	1.00	62.51
2449	N	ASN	564	17.281	20.194	37.278	1.00	62.12
2450	CA	ASN	564	16.596	21.312	36.741	1.00	63.12
2451	CB	ASN	564	15.703	20.918	35.651	1.00	63.80
2452	CG	ASN	564	16.263	21.124	34.284	1.00	60.00
2453	OD1	ASN	564	17.269	21.801	34.085	1.00	59.72
2454	ND2	ASN	564	15.577	20.559	33.311	1.00	61.08
2455	C	ASN	564	15.740	21.719	37.867	1.00	61.56
2456	O	ASN	564	15.204	22.818	37.863	1.00	61.14
2457	N	MET	565	15.483	20.798	38.768	1.00	63.63
2458	CA	MET	565	14.643	21.083	39.872	1.00	60.96
2459	CB	MET	565	14.164	19.773	40.504	1.00	61.63
2460	CG	MET	565	12.686	19.546	40.369	1.00	65.53
2461	SD	MET	565	12.013	20.320	38.903	1.00	61.09
2462	CE	MET	565	10.337	20.392	39.357	1.00	60.22
2463	C	MET	565	15.560	21.814	40.802	1.00	62.76
2464	O	MET	565	15.162	22.713	41.539	1.00	60.13
2465	N	LEU	566	16.826	21.447	40.746	1.00	62.63
2466	CA	LEU	566	17.794	22.101	41.590	1.00	58.73
2467	CB	LEU	566	19.007	21.188	41.764	1.00	59.94
2468	CG	LEU	566	20.381	21.435	42.410	1.00	60.09
2469	CD1	LEU	566	21.236	21.209	41.243	1.00	60.52
2470	CD2	LEU	566	20.687	22.805	43.045	1.00	59.08
2471	C	LEU	566	18.142	23.418	40.952	1.00	61.33
2472	O	LEU	566	18.373	24.398	41.652	1.00	61.14
2473	N	GLY	567	18.140	23.461	39.625	1.00	57.88
2474	CA	GLY	567	18.436	24.703	38.935	1.00	63.27
2475	C	GLY	567	17.469	25.785	39.351	1.00	60.49
2476	O	GLY	567	17.854	26.938	39.514	1.00	61.62
2477	N	GLY	568	16.206	25.412	39.526	1.00	63.72
2478	CA	GLY	568	15.212	26.382	39.936	1.00	60.34
2479	C	GLY	568	15.617	27.006	41.256	1.00	60.96
2480	O	GLY	568	15.913	28.195	41.332	1.00	61.39
2481	N	ARG	569	15.662	26.196	42.302	1.00	59.63
2482	CA	ARG	569	16.011	26.692	43.623	1.00	58.74
2483	CB	ARG	569	16.143	25.530	44.588	1.00	62.58
2484	CG	ARG	569	14.860	24.767	44.719	1.00	61.89
2485	CD	ARG	569	14.973	23.794	45.842	1.00	60.95

2486	NE	ARG	569	16.047	22.854	45.573	1.00	60.03
2487	CZ	ARG	569	16.734	22.229	46.513	1.00	60.68
2488	NH1	ARG	569	16.459	22.447	47.793	1.00	65.06
2489	NH2	ARG	569	17.697	21.391	46.169	1.00	63.36
2490	C	ARG	569	17.261	27.538	43.671	1.00	59.59
2491	O	ARG	569	17.395	28.397	44.539	1.00	58.49
2492	N	GLN	570	18.179	27.299	42.747	1.00	60.12
2493	CA	GLN	570	19.417	28.069	42.704	1.00	62.83
2494	CB	GLN	570	20.457	27.359	41.852	1.00	64.23
2495	CG	GLN	570	21.212	26.254	42.529	1.00	60.55
2496	CD	GLN	570	22.345	25.738	41.674	1.00	61.81
2497	OE1	GLN	570	23.046	24.818	42.067	1.00	60.88
2498	NE2	GLN	570	22.533	26.331	40.499	1.00	56.12
2499	C	GLN	570	19.195	29.462	42.135	1.00	59.62
2500	O	GLN	570	19.872	30.409	42.529	1.00	60.45
2501	N	VAL	571	18.273	29.571	41.182	1.00	64.99
2502	CA	VAL	571	17.953	30.851	40.576	1.00	62.98
2503	CB	VAL	571	17.141	30.653	39.278	1.00	62.20
2504	CG1	VAL	571	16.363	31.906	38.929	1.00	61.93
2505	CG2	VAL	571	18.090	30.312	38.140	1.00	61.13
2506	C	VAL	571	17.166	31.658	41.605	1.00	63.93
2507	O	VAL	571	17.379	32.865	41.763	1.00	65.46
2508	N	ILE	572	16.271	30.981	42.317	1.00	61.03
2509	CA	ILE	572	15.483	31.623	43.360	1.00	58.70
2510	CB	ILE	572	14.548	30.605	44.045	1.00	66.72
2511	CG2	ILE	572	14.006	31.169	45.350	1.00	58.22
2512	CG1	ILE	572	13.425	30.220	43.081	1.00	61.85
2513	CD1	ILE	572	12.411	29.251	43.663	1.00	61.02
2514	C	ILE	572	16.456	32.186	44.390	1.00	59.43
2515	O	ILE	572	16.240	33.257	44.948	1.00	61.61
2516	N	ALA	573	17.531	31.446	44.628	1.00	62.51
2517	CA	ALA	573	18.562	31.844	45.571	1.00	63.19
2518	CB	ALA	573	19.467	30.662	45.875	1.00	59.65
2519	C	ALA	573	19.390	32.994	45.016	1.00	60.08
2520	O	ALA	573	19.853	33.852	45.765	1.00	61.27
2521	N	ALA	574	19.573	33.004	43.700	1.00	62.86
2522	CA	ALA	574	20.350	34.039	43.027	1.00	62.91
2523	CB	ALA	574	20.500	33.690	41.553	1.00	60.40
2524	C	ALA	574	19.729	35.426	43.176	1.00	61.54
2525	O	ALA	574	20.402	36.441	42.977	1.00	62.14
2526	N	VAL	575	18.447	35.461	43.535	1.00	63.11
2527	CA	VAL	575	17.721	36.716	43.708	1.00	61.22
2528	CB	VAL	575	16.214	36.502	43.529	1.00	61.11
2529	CG1	VAL	575	15.500	37.835	43.568	1.00	63.45
2530	CG2	VAL	575	15.950	35.795	42.218	1.00	55.96
2531	C	VAL	575	17.970	37.386	45.063	1.00	61.67
2532	O	VAL	575	18.242	38.589	45.119	1.00	61.16
2533	N	LYS	576	17.866	36.618	46.148	1.00	63.44

2534	CA	LYS	576	18.103	37.169	47.477	1.00	61.90
2535	CB	LYS	576	17.913	36.120	48.576	1.00	60.65
2536	CG	LYS	576	16.569	35.385	48.633	1.00	62.95
2537	CD	LYS	576	16.370	34.812	50.045	1.00	61.64
2538	CE	LYS	576	15.453	33.594	50.101	1.00	61.27
2539	NZ	LYS	576	16.134	32.288	49.785	1.00	60.24
2540	C	LYS	576	19.554	37.616	47.498	1.00	62.75
2541	O	LYS	576	19.966	38.384	48.367	1.00	59.51
2542	N	TRP	577	20.320	37.103	46.534	1.00	64.04
2543	CA	TRP	577	21.741	37.407	46.382	1.00	63.24
2544	CB	TRP	577	22.447	36.277	45.610	1.00	61.04
2545	CG	TRP	577	23.852	36.613	45.166	1.00	62.92
2546	CD2	TRP	577	24.285	36.919	43.828	1.00	59.92
2547	CE2	TRP	577	25.663	37.212	43.892	1.00	60.22
2548	CE3	TRP	577	23.637	36.978	42.584	1.00	61.13
2549	CD1	TRP	577	24.956	36.729	45.958	1.00	63.10
2550	NE1	TRP	577	26.045	37.088	45.201	1.00	58.91
2551	CZ2	TRP	577	26.411	37.557	42.763	1.00	58.75
2552	CZ3	TRP	577	24.378	37.325	41.461	1.00	63.87
2553	CH2	TRP	577	25.754	37.611	41.559	1.00	60.61
2554	C	TRP	577	21.923	38.719	45.634	1.00	60.28
2555	O	TRP	577	22.654	39.597	46.083	1.00	61.57
2556	N	ALA	578	21.251	38.837	44.490	1.00	60.75
2557	CA	ALA	578	21.338	40.032	43.661	1.00	62.79
2558	CB	ALA	578	20.522	39.847	42.395	1.00	63.55
2559	C	ALA	578	20.869	41.274	44.409	1.00	60.84
2560	O	ALA	578	21.347	42.370	44.156	1.00	60.70
2561	N	LYS	579	19.937	41.105	45.339	1.00	62.74
2562	CA	LYS	579	19.423	42.234	46.107	1.00	60.13
2563	CB	LYS	579	18.016	41.900	46.640	1.00	60.85
2564	CG	LYS	579	16.969	41.709	45.532	1.00	61.81
2565	CD	LYS	579	15.725	40.942	45.986	1.00	61.28
2566	CE	LYS	579	14.910	41.704	47.020	1.00	61.64
2567	NZ	LYS	579	13.708	40.953	47.492	1.00	62.20
2568	C	LYS	579	20.372	42.613	47.252	1.00	60.67
2569	O	LYS	579	20.251	43.683	47.835	1.00	59.96
2570	N	ALA	580	21.322	41.738	47.564	1.00	59.98
2571	CA	ALA	580	22.288	42.011	48.630	1.00	60.27
2572	CB	ALA	580	22.721	40.713	49.304	1.00	64.73
2573	C	ALA	580	23.505	42.722	48.059	1.00	58.96
2574	O	ALA	580	24.349	43.229	48.801	1.00	61.59
2575	N	ILE	581	23.590	42.738	46.731	1.00	63.39
2576	CA	ILE	581	24.690	43.380	46.030	1.00	60.52
2577	CB	ILE	581	24.789	42.908	44.559	1.00	60.74
2578	CG2	ILE	581	25.911	43.650	43.840	1.00	63.37
2579	CG1	ILE	581	25.069	41.409	44.494	1.00	60.26
2580	CD1	ILE	581	24.930	40.862	43.091	1.00	61.59
2581	C	ILE	581	24.426	44.873	46.025	1.00	63.62

2582	O	ILE	581	23.418	45.329	45.482	1.00	63.59
2583	N	PRO	582	25.329	45.655	46.634	1.00	62.76
2584	CD	PRO	582	26.596	45.257	47.270	1.00	63.28
2585	CA	PRO	582	25.162	47.104	46.681	1.00	64.52
2586	CB	PRO	582	26.505	47.589	47.226	1.00	62.45
2587	CG	PRO	582	26.934	46.473	48.106	1.00	59.21
2588	C	PRO	582	24.882	47.654	45.298	1.00	62.22
2589	O	PRO	582	25.518	47.252	44.323	1.00	61.69
2590	N	GLY	583	23.913	48.560	45.224	1.00	58.26
2591	CA	GLY	583	23.565	49.189	43.965	1.00	59.81
2592	C	GLY	583	22.640	48.446	43.028	1.00	61.92
2593	O	GLY	583	22.231	49.002	42.024	1.00	58.88
2594	N	PHE	584	22.302	47.201	43.327	1.00	62.92
2595	CA	PHE	584	21.418	46.459	42.438	1.00	61.83
2596	CB	PHE	584	21.563	44.953	42.677	1.00	62.46
2597	CG	PHE	584	20.863	44.104	41.650	1.00	57.96
2598	CD1	PHE	584	21.406	43.921	40.390	1.00	63.14
2599	CD2	PHE	584	19.646	43.514	41.938	1.00	62.84
2600	CE1	PHE	584	20.746	43.166	39.437	1.00	61.42
2601	CE2	PHE	584	18.980	42.759	40.991	1.00	60.47
2602	CZ	PHE	584	19.533	42.585	39.737	1.00	59.28
2603	C	PHE	584	19.958	46.883	42.624	1.00	60.13
2604	O	PHE	584	19.210	46.996	41.653	1.00	61.49
2605	N	ARG	585	19.561	47.131	43.870	1.00	60.78
2606	CA	ARG	585	18.190	47.535	44.160	1.00	63.10
2607	CB	ARG	585	17.832	47.252	45.627	1.00	59.03
2608	CG	ARG	585	17.716	45.757	45.943	1.00	57.77
2609	CD	ARG	585	17.222	45.476	47.365	1.00	61.69
2610	NE	ARG	585	15.825	45.858	47.587	1.00	62.10
2611	CZ	ARG	585	14.800	45.492	46.817	1.00	62.77
2612	NH1	ARG	585	14.996	44.724	45.744	1.00	60.63
2613	NH2	ARG	585	13.569	45.893	47.126	1.00	59.26
2614	C	ARG	585	17.952	48.996	43.843	1.00	59.85
2615	O	ARG	585	16.833	49.487	43.965	1.00	61.84
2616	N	ASN	586	19.003	49.689	43.424	1.00	60.92
2617	CA	ASN	586	18.871	51.094	43.090	1.00	62.56
2618	CB	ASN	586	19.987	51.892	43.740	1.00	59.81
2619	CG	ASN	586	20.079	51.620	45.218	1.00	62.07
2620	OD1	ASN	586	20.714	50.651	45.641	1.00	62.28
2621	ND2	ASN	586	19.415	52.452	46.018	1.00	56.67
2622	C	ASN	586	18.865	51.271	41.592	1.00	63.34
2623	O	ASN	586	19.054	52.363	41.068	1.00	60.96
2624	N	LEU	587	18.648	50.163	40.907	1.00	62.25
2625	CA	LEU	587	18.551	50.166	39.467	1.00	60.33
2626	CB	LEU	587	19.304	48.971	38.887	1.00	63.97
2627	CG	LEU	587	20.823	49.075	38.847	1.00	59.84
2628	CD1	LEU	587	21.410	47.701	38.948	1.00	62.41
2629	CD2	LEU	587	21.262	49.748	37.572	1.00	64.48

2630	C	LEU	587	17.053	50.008	39.259	1.00	61.19
2631	O	LEU	587	16.355	49.541	40.164	1.00	61.87
2632	N	HIS	588	16.556	50.400	38.090	1.00	63.05
2633	CA	HIS	588	15.130	50.288	37.829	1.00	58.93
2634	CB	HIS	588	14.797	50.621	36.371	1.00	62.93
2635	CG	HIS	588	13.338	50.871	36.131	1.00	61.44
2636	CD2	HIS	588	12.679	51.990	35.745	1.00	61.68
2637	ND1	HIS	588	12.369	49.912	36.344	1.00	59.82
2638	CE1	HIS	588	11.178	50.431	36.101	1.00	59.25
2639	NE2	HIS	588	11.339	51.691	35.736	1.00	58.14
2640	C	HIS	588	14.723	48.860	38.128	1.00	61.41
2641	O	HIS	588	15.515	47.942	37.948	1.00	59.96
2642	N	LEU	589	13.492	48.686	38.598	1.00	59.88
2643	CA	LEU	589	12.974	47.370	38.929	1.00	61.54
2644	CB	LEU	589	11.602	47.509	39.599	1.00	60.80
2645	CG	LEU	589	10.980	46.337	40.367	1.00	62.36
2646	CD1	LEU	589	10.643	45.192	39.424	1.00	59.67
2647	CD2	LEU	589	11.934	45.887	41.449	1.00	61.30
2648	C	LEU	589	12.867	46.562	37.640	1.00	60.73
2649	O	LEU	589	12.841	45.332	37.667	1.00	59.26
2650	N	ASP	590	12.811	47.254	36.507	1.00	62.77
2651	CA	ASP	590	12.714	46.574	35.222	1.00	59.61
2652	CB	ASP	590	12.172	47.516	34.154	1.00	60.63
2653	CG	ASP	590	10.676	47.476	34.060	1.00	60.64
2654	OD1	ASP	590	10.031	47.099	35.060	1.00	66.03
2655	OD2	ASP	590	10.140	47.830	32.989	1.00	62.74
2656	C	ASP	590	14.077	46.079	34.801	1.00	64.03
2657	O	ASP	590	14.194	45.131	34.020	1.00	61.02
2658	N	ASP	591	15.109	46.734	35.319	1.00	61.76
2659	CA	ASP	591	16.481	46.364	34.993	1.00	61.72
2660	CB	ASP	591	17.425	47.557	35.224	1.00	60.28
2661	CG	ASP	591	17.174	48.709	34.250	1.00	66.48
2662	OD1	ASP	591	16.782	48.445	33.092	1.00	56.28
2663	OD2	ASP	591	17.393	49.877	34.639	1.00	63.43
2664	C	ASP	591	16.937	45.160	35.813	1.00	60.81
2665	O	ASP	591	17.642	44.292	35.306	1.00	61.99
2666	N	GLN	592	16.515	45.120	37.075	1.00	59.60
2667	CA	GLN	592	16.852	44.035	37.981	1.00	59.54
2668	CB	GLN	592	16.145	44.209	39.327	1.00	60.92
2669	CG	GLN	592	16.268	45.571	39.962	1.00	63.19
2670	CD	GLN	592	15.991	45.536	41.460	1.00	61.96
2671	OE1	GLN	592	15.303	44.641	41.967	1.00	59.41
2672	NE2	GLN	592	16.522	46.518	42.176	1.00	61.73
2673	C	GLN	592	16.409	42.711	37.376	1.00	58.77
2674	O	GLN	592	17.034	41.668	37.606	1.00	60.09
2675	N	MET	593	15.319	42.762	36.611	1.00	61.89
2676	CA	MET	593	14.756	41.575	35.977	1.00	60.29
2677	CB	MET	593	13.257	41.746	35.768	1.00	61.65

2678	CG	MET	593	12.401	41.411	36.969	1.00	61.69
2679	SD	MET	593	10.676	41.232	36.456	1.00	62.68
2680	CE	MET	593	10.249	42.940	36.274	1.00	60.78
2681	C	MET	593	15.388	41.229	34.645	1.00	59.77
2682	O	MET	593	15.386	40.068	34.241	1.00	61.16
2683	N	THR	594	15.904	42.235	33.948	1.00	59.97
2684	CA	THR	594	16.541	42.008	32.655	1.00	61.96
2685	CB	THR	594	16.828	43.335	31.932	1.00	61.57
2686	OG1	THR	594	15.726	44.234	32.127	1.00	61.11
2687	CG2	THR	594	17.026	43.086	30.435	1.00	62.41
2688	C	THR	594	17.865	41.305	32.902	1.00	63.83
2689	O	THR	594	18.184	40.287	32.274	1.00	62.47
2690	N	LEU	595	18.634	41.865	33.829	1.00	61.96
2691	CA	LEU	595	19.924	41.308	34.184	1.00	62.86
2692	CB	LEU	595	20.585	42.172	35.265	1.00	61.42
2693	CG	LEU	595	20.937	43.615	34.885	1.00	63.11
2694	CD1	LEU	595	21.680	44.276	36.031	1.00	63.10
2695	CD2	LEU	595	21.791	43.634	33.636	1.00	59.45
2696	C	LEU	595	19.784	39.859	34.660	1.00	61.56
2697	O	LEU	595	20.438	38.960	34.136	1.00	62.15
2698	N	LEU	596	18.920	39.629	35.640	1.00	63.33
2699	CA	LEU	596	18.728	38.283	36.156	1.00	61.25
2700	CB	LEU	596	17.830	38.313	37.387	1.00	59.50
2701	CG	LEU	596	18.518	38.469	38.735	1.00	63.65
2702	CD1	LEU	596	17.484	38.837	39.769	1.00	60.39
2703	CD2	LEU	596	19.232	37.190	39.109	1.00	62.18
2704	C	LEU	596	18.159	37.293	35.140	1.00	57.46
2705	O	LEU	596	18.306	36.079	35.310	1.00	60.98
2706	N	GLN	597	17.507	37.800	34.095	1.00	60.24
2707	CA	GLN	597	16.915	36.953	33.055	1.00	59.39
2708	CB	GLN	597	15.727	37.660	32.413	1.00	63.86
2709	CG	GLN	597	14.431	37.528	33.171	1.00	63.29
2710	CD	GLN	597	13.365	38.466	32.648	1.00	58.84
2711	OE1	GLN	597	13.389	38.873	31.484	1.00	61.11
2712	NE2	GLN	597	12.414	38.811	33.505	1.00	60.83
2713	C	GLN	597	17.927	36.620	31.973	1.00	60.76
2714	O	GLN	597	17.829	35.597	31.302	1.00	63.58
2715	N	TYR	598	18.900	37.501	31.806	1.00	59.20
2716	CA	TYR	598	19.923	37.315	30.807	1.00	61.48
2717	CB	TYR	598	20.378	38.678	30.311	1.00	64.95
2718	CG	TYR	598	19.364	39.407	29.466	1.00	59.33
2719	CD1	TYR	598	18.119	38.844	29.177	1.00	59.16
2720	CE1	TYR	598	17.213	39.496	28.344	1.00	62.34
2721	CD2	TYR	598	19.673	40.645	28.903	1.00	58.48
2722	CE2	TYR	598	18.771	41.303	28.067	1.00	61.12
2723	CZ	TYR	598	17.551	40.721	27.794	1.00	63.18
2724	OH	TYR	598	16.680	41.371	26.960	1.00	63.83
2725	C	TYR	598	21.130	36.532	31.320	1.00	63.31

2726	O	TYR	598	21.850	35.900	30.550	1.00	62.59
2727	N	SER	599	21.356	36.554	32.623	1.00	62.16
2728	CA	SER	599	22.511	35.859	33.157	1.00	62.80
2729	CB	SER	599	23.420	36.885	33.845	1.00	60.71
2730	OG	SER	599	22.660	37.845	34.560	1.00	60.75
2731	C	SER	599	22.245	34.678	34.093	1.00	60.81
2732	O	SER	599	23.183	34.104	34.636	1.00	57.53
2733	N	TRP	600	20.986	34.293	34.272	1.00	62.86
2734	CA	TRP	600	20.683	33.187	35.180	1.00	60.85
2735	CB	TRP	600	19.186	32.813	35.134	1.00	60.84
2736	CG	TRP	600	18.745	32.104	33.887	1.00	61.86
2737	CD2	TRP	600	18.561	30.697	33.726	1.00	61.60
2738	CE2	TRP	600	18.300	30.461	32.362	1.00	64.40
2739	CE3	TRP	600	18.599	29.611	34.602	1.00	59.75
2740	CD1	TRP	600	18.574	32.653	32.650	1.00	60.08
2741	NE1	TRP	600	18.311	31.672	31.724	1.00	59.13
2742	CZ2	TRP	600	18.085	29.182	31.854	1.00	61.82
2743	CZ3	TRP	600	18.383	28.342	34.097	1.00	63.01
2744	CH2	TRP	600	18.131	28.137	32.737	1.00	62.11
2745	C	TRP	600	21.523	31.963	34.848	1.00	61.75
2746	O	TRP	600	21.973	31.238	35.732	1.00	60.91
2747	N	MET	601	21.761	31.749	33.564	1.00	62.84
2748	CA	MET	601	22.504	30.591	33.172	1.00	60.19
2749	CB	MET	601	22.084	30.133	31.794	1.00	61.93
2750	CG	MET	601	22.616	28.786	31.496	1.00	63.07
2751	SD	MET	601	21.595	27.427	31.465	1.00	62.35
2752	CE	MET	601	22.357	26.773	32.529	1.00	60.74
2753	C	MET	601	24.008	30.766	33.243	1.00	61.35
2754	O	MET	601	24.732	29.790	33.391	1.00	62.01
2755	N	SER	602	24.483	32.002	33.146	1.00	59.64
2756	CA	SER	602	25.914	32.253	33.227	1.00	61.85
2757	CB	SER	602	26.249	33.637	32.675	1.00	63.12
2758	OG	SER	602	27.643	33.887	32.746	1.00	63.90
2759	C	SER	602	26.356	32.163	34.684	1.00	63.19
2760	O	SER	602	27.478	31.765	34.976	1.00	59.89
2761	N	LEU	603	25.452	32.537	35.588	1.00	59.89
2762	CA	LEU	603	25.703	32.527	37.027	1.00	63.05
2763	CB	LEU	603	24.673	33.413	37.748	1.00	60.06
2764	CG	LEU	603	24.752	34.936	37.606	1.00	58.80
2765	CD1	LEU	603	23.591	35.588	38.334	1.00	59.17
2766	CD2	LEU	603	26.051	35.422	38.175	1.00	63.89
2767	C	LEU	603	25.624	31.118	37.586	1.00	60.06
2768	O	LEU	603	26.337	30.753	38.519	1.00	58.30
2769	N	MET	604	24.745	30.323	37.004	1.00	62.50
2770	CA	MET	604	24.565	28.967	37.468	1.00	61.20
2771	CB	MET	604	23.151	28.541	37.166	1.00	59.34
2772	CG	MET	604	22.185	28.879	38.247	1.00	61.83
2773	SD	MET	604	22.610	30.141	39.388	1.00	62.09

2774	CE	MET	604	22.173	29.285	40.731	1.00	60.68
2775	C	MET	604	25.578	28.009	36.879	1.00	61.48
2776	O	MET	604	25.989	27.048	37.536	1.00	60.91
2777	N	ALA	605	25.988	28.292	35.646	1.00	58.39
2778	CA	ALA	605	26.970	27.493	34.943	1.00	62.30
2779	CB	ALA	605	26.934	27.812	33.472	1.00	63.55
2780	C	ALA	605	28.341	27.820	35.502	1.00	63.47
2781	O	ALA	605	29.194	26.944	35.590	1.00	60.63
2782	N	PHE	606	28.546	29.082	35.882	1.00	60.75
2783	CA	PHE	606	29.832	29.536	36.411	1.00	62.24
2784	CB	PHE	606	29.951	31.059	36.300	1.00	65.41
2785	CG	PHE	606	31.316	31.606	36.663	1.00	64.45
2786	CD1	PHE	606	32.424	31.375	35.848	1.00	62.88
2787	CD2	PHE	606	31.483	32.388	37.802	1.00	61.45
2788	CE1	PHE	606	33.668	31.919	36.162	1.00	61.89
2789	CE2	PHE	606	32.725	32.931	38.120	1.00	63.04
2790	CZ	PHE	606	33.814	32.696	37.296	1.00	66.17
2791	C	PHE	606	30.044	29.121	37.851	1.00	64.34
2792	O	PHE	606	31.154	28.764	38.234	1.00	61.04
2793	N	ALA	607	28.997	29.180	38.661	1.00	59.38
2794	CA	ALA	607	29.144	28.771	40.047	1.00	61.90
2795	CB	ALA	607	27.953	29.224	40.865	1.00	58.55
2796	C	ALA	607	29.269	27.246	40.073	1.00	58.23
2797	O	ALA	607	29.912	26.681	40.953	1.00	60.68
2798	N	LEU	608	28.656	26.571	39.110	1.00	61.24
2799	CA	LEU	608	28.771	25.121	39.086	1.00	60.02
2800	CB	LEU	608	27.928	24.526	37.958	1.00	62.86
2801	CG	LEU	608	27.703	23.018	37.693	1.00	60.90
2802	CD1	LEU	608	27.926	22.923	36.222	1.00	62.46
2803	CD2	LEU	608	28.630	22.033	38.439	1.00	60.02
2804	C	LEU	608	30.240	24.783	38.858	1.00	61.60
2805	O	LEU	608	30.758	23.870	39.479	1.00	62.78
2806	N	GLY	609	30.917	25.511	37.974	1.00	63.89
2807	CA	GLY	609	32.319	25.229	37.746	1.00	60.11
2808	C	GLY	609	33.143	25.391	39.018	1.00	61.05
2809	O	GLY	609	34.080	24.631	39.266	1.00	62.95
2810	N	TRP	610	32.783	26.374	39.838	1.00	62.51
2811	CA	TRP	610	33.499	26.652	41.073	1.00	63.33
2812	CB	TRP	610	32.917	27.885	41.741	1.00	59.08
2813	CG	TRP	610	33.617	28.226	43.008	1.00	60.29
2814	CD2	TRP	610	34.910	28.821	43.127	1.00	61.56
2815	CE2	TRP	610	35.194	28.930	44.501	1.00	59.81
2816	CE3	TRP	610	35.860	29.273	42.200	1.00	57.77
2817	CD1	TRP	610	33.178	28.002	44.279	1.00	61.04
2818	NE1	TRP	610	34.121	28.423	45.183	1.00	63.24
2819	CZ2	TRP	610	36.387	29.472	44.973	1.00	58.16
2820	CZ3	TRP	610	37.048	29.811	42.670	1.00	62.09
2821	CH2	TRP	610	37.301	29.905	44.043	1.00	63.07

2822	C	TRP	610	33.516	25.510	42.073	1.00	62.56
2823	O	TRP	610	34.554	25.205	42.662	1.00	62.85
2824	N	ARG	611	32.360	24.896	42.288	1.00	64.01
2825	CA	ARG	611	32.268	23.784	43.222	1.00	61.00
2826	CB	ARG	611	30.803	23.396	43.440	1.00	60.82
2827	CG	ARG	611	29.973	24.437	44.180	1.00	60.63
2828	CD	ARG	611	28.568	23.899	44.480	1.00	63.65
2829	NE	ARG	611	27.830	23.608	43.250	1.00	60.05
2830	CZ	ARG	611	27.228	24.528	42.498	1.00	61.48
2831	NH1	ARG	611	27.255	25.811	42.853	1.00	62.30
2832	NH2	ARG	611	26.638	24.175	41.365	1.00	62.30
2833	C	ARG	611	33.049	22.606	42.648	1.00	64.56
2834	O	ARG	611	33.712	21.854	43.373	1.00	59.80
2835	N	SER	612	32.971	22.467	41.329	1.00	60.03
2836	CA	SER	612	33.664	21.403	40.624	1.00	62.69
2837	CB	SER	612	33.312	21.451	39.141	1.00	60.54
2838	OG	SER	612	31.976	21.038	38.947	1.00	61.90
2839	C	SER	612	35.163	21.542	40.815	1.00	60.18
2840	O	SER	612	35.842	20.597	41.209	1.00	62.35
2841	N	TYR	613	35.663	22.738	40.538	1.00	59.25
2842	CA	TYR	613	37.074	23.058	40.677	1.00	60.56
2843	CB	TYR	613	37.265	24.534	40.311	1.00	63.42
2844	CG	TYR	613	38.515	25.215	40.829	1.00	66.04
2845	CD1	TYR	613	39.771	24.631	40.692	1.00	61.54
2846	CE1	TYR	613	40.925	25.308	41.091	1.00	59.89
2847	CD2	TYR	613	38.443	26.491	41.384	1.00	61.40
2848	CE2	TYR	613	39.586	27.172	41.782	1.00	60.60
2849	CZ	TYR	613	40.823	26.577	41.633	1.00	61.69
2850	OH	TYR	613	41.950	27.258	42.022	1.00	57.50
2851	C	TYR	613	37.624	22.765	42.074	1.00	61.96
2852	O	TYR	613	38.665	22.130	42.219	1.00	62.16
2853	N	ARG	614	36.913	23.204	43.102	1.00	65.05
2854	CA	ARG	614	37.380	23.004	44.463	1.00	59.34
2855	CB	ARG	614	36.724	24.017	45.395	1.00	60.68
2856	CG	ARG	614	36.950	25.445	45.007	1.00	63.19
2857	CD	ARG	614	36.724	26.354	46.190	1.00	59.94
2858	NE	ARG	614	37.945	26.927	46.773	1.00	59.42
2859	CZ	ARG	614	39.115	27.068	46.145	1.00	60.26
2860	NH1	ARG	614	40.141	27.628	46.776	1.00	60.62
2861	NH2	ARG	614	39.288	26.619	44.906	1.00	59.69
2862	C	ARG	614	37.144	21.620	45.019	1.00	60.75
2863	O	ARG	614	37.899	21.144	45.869	1.00	61.95
2864	N	GLN	615	36.093	20.967	44.549	1.00	60.97
2865	CA	GLN	615	35.780	19.654	45.074	1.00	61.36
2866	CB	GLN	615	34.282	19.387	44.957	1.00	59.74
2867	CG	GLN	615	33.666	18.942	46.273	1.00	65.30
2868	CD	GLN	615	32.416	18.106	46.097	1.00	64.80
2869	OE1	GLN	615	32.019	17.380	47.007	1.00	59.65

2870	NE2	GLN	615	31.787	18.204	44.928	1.00	63.88
2871	C	GLN	615	36.547	18.523	44.419	1.00	61.87
2872	O	GLN	615	36.984	17.588	45.093	1.00	61.19
2873	N	SER	616	36.726	18.615	43.109	1.00	62.69
2874	CA	SER	616	37.408	17.559	42.387	1.00	60.64
2875	CB	SER	616	36.380	16.632	41.757	1.00	64.46
2876	OG	SER	616	35.731	17.299	40.688	1.00	63.47
2877	C	SER	616	38.347	18.047	41.298	1.00	59.36
2878	O	SER	616	38.444	17.424	40.246	1.00	61.79
2879	N	SER	617	39.021	19.163	41.534	1.00	62.74
2880	CA	SER	617	39.972	19.681	40.560	1.00	60.01
2881	CB	SER	617	41.253	18.847	40.638	1.00	56.86
2882	OG	SER	617	41.690	18.714	41.980	1.00	64.58
2883	C	SER	617	39.433	19.675	39.119	1.00	62.31
2884	O	SER	617	40.099	19.196	38.196	1.00	60.08
2885	N	ALA	618	38.230	20.213	38.931	1.00	62.60
2886	CA	ALA	618	37.600	20.261	37.612	1.00	62.84
2887	CB	ALA	618	38.399	21.165	36.676	1.00	61.64
2888	C	ALA	618	37.475	18.866	37.005	1.00	60.94
2889	O	ALA	618	37.175	18.725	35.820	1.00	63.12
2890	N	ASN	619	37.692	17.836	37.820	1.00	60.02
2891	CA	ASN	619	37.610	16.465	37.330	1.00	60.02
2892	CB	ASN	619	38.467	15.523	38.178	1.00	61.65
2893	CG	ASN	619	39.881	15.426	37.663	1.00	65.19
2894	OD1	ASN	619	40.813	15.986	38.241	1.00	58.62
2895	ND2	ASN	619	40.047	14.729	36.547	1.00	59.93
2896	C	ASN	619	36.205	15.922	37.241	1.00	63.97
2897	O	ASN	619	35.933	15.005	36.469	1.00	61.24
2898	N	LEU	620	35.305	16.487	38.028	1.00	61.46
2899	CA	LEU	620	33.925	16.044	37.999	1.00	61.85
2900	CB	LEU	620	33.599	15.266	39.271	1.00	63.36
2901	CG	LEU	620	34.516	14.087	39.589	1.00	60.08
2902	CD1	LEU	620	33.992	13.354	40.805	1.00	65.17
2903	CD2	LEU	620	34.578	13.145	38.408	1.00	59.21
2904	C	LEU	620	33.031	17.266	37.890	1.00	63.79
2905	O	LEU	620	33.520	18.400	37.844	1.00	62.56
2906	N	LEU	621	31.728	17.022	37.808	1.00	60.88
2907	CA	LEU	621	30.757	18.096	37.739	1.00	60.93
2908	CB	LEU	621	29.822	17.930	36.545	1.00	59.84
2909	CG	LEU	621	30.365	18.564	35.272	1.00	61.52
2910	CD1	LEU	621	29.302	18.516	34.204	1.00	61.79
2911	CD2	LEU	621	30.776	19.998	35.547	1.00	62.82
2912	C	LEU	621	30.001	17.973	39.033	1.00	59.84
2913	O	LEU	621	29.267	17.009	39.249	1.00	59.39
2914	N	CYS	622	30.191	18.952	39.903	1.00	60.82
2915	CA	CYS	622	29.562	18.902	41.201	1.00	61.70
2916	CB	CYS	622	30.612	19.216	42.276	1.00	61.70
2917	SG	CYS	622	32.249	18.417	42.005	1.00	55.72

2918	C	CYS	622	28.360	19.822	41.333	1.00	60.92
2919	O	CYS	622	28.394	20.777	42.107	1.00	60.85
2920	N	PHE	623	27.299	19.518	40.584	1.00	62.83
2921	CA	PHE	623	26.057	20.298	40.618	1.00	61.52
2922	CB	PHE	623	24.944	19.578	39.827	1.00	63.16
2923	CG	PHE	623	25.174	19.562	38.332	1.00	64.30
2924	CD1	PHE	623	25.946	18.565	37.734	1.00	62.97
2925	CD2	PHE	623	24.667	20.580	37.527	1.00	59.44
2926	CE1	PHE	623	26.214	18.585	36.354	1.00	60.51
2927	CE2	PHE	623	24.931	20.607	36.152	1.00	61.00
2928	CZ	PHE	623	25.705	19.609	35.566	1.00	58.20
2929	C	PHE	623	25.631	20.512	42.074	1.00	62.99
2930	O	PHE	623	25.433	21.650	42.520	1.00	59.63
2931	N	ALA	624	25.489	19.404	42.798	1.00	60.19
2932	CA	ALA	624	25.146	19.426	44.220	1.00	60.71
2933	CB	ALA	624	23.953	18.540	44.505	1.00	65.97
2934	C	ALA	624	26.384	18.877	44.921	1.00	60.87
2935	O	ALA	624	27.278	18.328	44.276	1.00	61.88
2936	N	PRO	625	26.467	19.023	46.248	1.00	63.71
2937	CD	PRO	625	25.561	19.666	47.207	1.00	59.14
2938	CA	PRO	625	27.658	18.496	46.924	1.00	61.58
2939	CB	PRO	625	27.528	19.055	48.346	1.00	64.33
2940	CG	PRO	625	26.534	20.184	48.212	1.00	61.92
2941	C	PRO	625	27.593	16.960	46.904	1.00	61.41
2942	O	PRO	625	28.630	16.280	46.869	1.00	60.49
2943	N	ASP	626	26.353	16.450	46.913	1.00	61.38
2944	CA	ASP	626	26.036	15.016	46.914	1.00	61.12
2945	CB	ASP	626	25.050	14.730	48.038	1.00	59.24
2946	CG	ASP	626	23.643	15.219	47.706	1.00	60.93
2947	OD1	ASP	626	23.518	16.271	47.036	1.00	62.15
2948	OD2	ASP	626	22.658	14.564	48.112	1.00	64.40
2949	C	ASP	626	25.405	14.562	45.587	1.00	62.42
2950	O	ASP	626	24.526	13.703	45.568	1.00	60.54
2951	N	LEU	627	25.834	15.152	44.483	1.00	60.30
2952	CA	LEU	627	25.293	14.792	43.183	1.00	61.38
2953	CB	LEU	627	24.007	15.569	42.915	1.00	59.07
2954	CG	LEU	627	23.311	15.347	41.573	1.00	62.30
2955	CD1	LEU	627	22.632	13.994	41.525	1.00	59.92
2956	CD2	LEU	627	22.300	16.440	41.381	1.00	64.94
2957	C	LEU	627	26.349	15.143	42.152	1.00	59.24
2958	O	LEU	627	26.321	16.224	41.550	1.00	60.06
2959	N	ILE	628	27.284	14.219	41.958	1.00	59.89
2960	CA	ILE	628	28.380	14.422	41.030	1.00	60.40
2961	CB	ILE	628	29.729	14.056	41.692	1.00	62.59
2962	CG2	ILE	628	30.850	14.267	40.716	1.00	59.44
2963	CG1	ILE	628	29.990	14.940	42.909	1.00	61.86
2964	CD1	ILE	628	29.045	14.711	44.049	1.00	62.51
2965	C	ILE	628	28.234	13.609	39.750	1.00	64.22

2966	O	ILE	628	28.028	12.402	39.787	1.00	60.75
2967	N	ILE	629	28.323	14.272	38.608	1.00	60.54
2968	CA	ILE	629	28.239	13.540	37.370	1.00	62.37
2969	CB	ILE	629	28.044	14.470	36.165	1.00	65.41
2970	CG2	ILE	629	28.371	13.733	34.877	1.00	61.37
2971	CG1	ILE	629	26.619	15.024	36.170	1.00	63.05
2972	CD1	ILE	629	25.623	14.193	36.983	1.00	60.63
2973	C	ILE	629	29.575	12.839	37.270	1.00	60.22
2974	O	ILE	629	30.580	13.454	36.929	1.00	58.35
2975	N	ASN	630	29.580	11.556	37.611	1.00	60.04
2976	CA	ASN	630	30.776	10.726	37.570	1.00	60.83
2977	CB	ASN	630	30.674	9.637	38.632	1.00	62.77
2978	CG	ASN	630	29.368	8.868	38.556	1.00	60.79
2979	OD1	ASN	630	29.051	8.248	37.541	1.00	61.32
2980	ND2	ASN	630	28.603	8.908	39.632	1.00	62.90
2981	C	ASN	630	30.949	10.085	36.197	1.00	60.61
2982	O	ASN	630	30.016	10.041	35.403	1.00	62.50
2983	N	GLU	631	32.151	9.592	35.926	1.00	63.77
2984	CA	GLU	631	32.472	8.954	34.653	1.00	60.65
2985	CB	GLU	631	33.804	8.219	34.786	1.00	62.06
2986	CG	GLU	631	34.021	7.046	33.841	1.00	63.14
2987	CD	GLU	631	35.255	6.229	34.232	1.00	59.80
2988	OE1	GLU	631	36.349	6.836	34.405	1.00	61.43
2989	OE2	GLU	631	35.122	4.988	34.369	1.00	58.68
2990	C	GLU	631	31.381	7.986	34.254	1.00	61.07
2991	O	GLU	631	30.879	8.014	33.132	1.00	61.02
2992	N	GLN	632	31.011	7.126	35.186	1.00	63.77
2993	CA	GLN	632	29.978	6.151	34.916	1.00	61.66
2994	CB	GLN	632	29.732	5.285	36.159	1.00	61.41
2995	CG	GLN	632	30.936	4.415	36.579	1.00	65.26
2996	CD	GLN	632	31.704	3.828	35.393	1.00	64.37
2997	OE1	GLN	632	31.109	3.357	34.420	1.00	60.73
2998	NE2	GLN	632	33.034	3.847	35.480	1.00	59.46
2999	C	GLN	632	28.695	6.851	34.466	1.00	61.12
3000	O	GLN	632	28.055	6.417	33.512	1.00	62.13
3001	N	ARG	633	28.334	7.946	35.134	1.00	59.27
3002	CA	ARG	633	27.125	8.682	34.767	1.00	61.29
3003	CB	ARG	633	26.821	9.786	35.775	1.00	59.65
3004	CG	ARG	633	26.235	9.274	37.069	1.00	62.42
3005	CD	ARG	633	25.223	10.258	37.602	1.00	60.12
3006	NE	ARG	633	24.486	9.732	38.743	1.00	61.79
3007	CZ	ARG	633	24.739	10.038	40.011	1.00	64.89
3008	NH1	ARG	633	25.717	10.878	40.308	1.00	60.64
3009	NH2	ARG	633	24.014	9.501	40.984	1.00	62.92
3010	C	ARG	633	27.151	9.274	33.360	1.00	61.86
3011	O	ARG	633	26.086	9.401	32.750	1.00	59.63
3012	N	MET	634	28.337	9.643	32.855	1.00	64.70
3013	CA	MET	634	28.465	10.180	31.497	1.00	60.91

3014	CB	MET	634	29.921	10.556	31.189	1.00	59.90
3015	CG	MET	634	30.438	11.791	31.950	1.00	60.63
3016	SD	MET	634	30.042	13.425	31.192	1.00	60.35
3017	CE	MET	634	30.985	14.531	32.251	1.00	64.03
3018	C	MET	634	27.956	9.086	30.543	1.00	60.81
3019	O	MET	634	28.727	8.350	29.899	1.00	62.71
3020	N	THR	635	26.622	8.989	30.531	1.00	62.02
3021	CA	THR	635	25.820	8.059	29.738	1.00	62.69
3022	CB	THR	635	24.313	8.140	30.124	1.00	62.75
3023	OG1	THR	635	24.150	7.893	31.528	1.00	60.63
3024	CG2	THR	635	23.486	7.141	29.303	1.00	61.43
3025	C	THR	635	25.912	8.531	28.307	1.00	61.30
3026	O	THR	635	26.510	7.876	27.454	1.00	59.84
3027	N	LEU	636	25.315	9.694	28.077	1.00	61.92
3028	CA	LEU	636	25.270	10.317	26.765	1.00	60.40
3029	CB	LEU	636	23.901	10.968	26.586	1.00	63.75
3030	CG	LEU	636	22.679	10.156	26.167	1.00	61.04
3031	CD1	LEU	636	22.623	8.760	26.811	1.00	59.92
3032	CD2	LEU	636	21.476	11.011	26.536	1.00	55.92
3033	C	LEU	636	26.347	11.377	26.441	1.00	63.57
3034	O	LEU	636	26.834	12.087	27.327	1.00	58.28
3035	N	PRO	637	26.754	11.471	25.155	1.00	61.79
3036	CD	PRO	637	26.479	10.631	23.987	1.00	63.46
3037	CA	PRO	637	27.744	12.476	24.794	1.00	60.89
3038	CB	PRO	637	28.363	11.932	23.490	1.00	63.07
3039	CG	PRO	637	27.855	10.482	23.398	1.00	62.95
3040	C	PRO	637	26.780	13.647	24.551	1.00	61.80
3041	O	PRO	637	27.038	14.531	23.736	1.00	60.33
3042	N	CYS	638	25.605	13.523	25.193	1.00	63.35
3043	CA	CYS	638	24.557	14.549	25.225	1.00	58.89
3044	CB	CYS	638	23.122	14.023	25.351	1.00	62.48
3045	SG	CYS	638	22.633	12.668	24.333	1.00	61.93
3046	C	CYS	638	24.925	14.896	26.642	1.00	59.34
3047	O	CYS	638	25.366	16.010	26.968	1.00	61.64
3048	N	MET	639	24.773	13.878	27.486	1.00	59.95
3049	CA	MET	639	25.094	14.058	28.870	1.00	62.51
3050	CB	MET	639	24.794	12.794	29.647	1.00	56.25
3051	CG	MET	639	24.597	13.021	31.126	1.00	59.11
3052	SD	MET	639	23.446	14.225	31.808	1.00	60.73
3053	CE	MET	639	24.286	14.281	33.307	1.00	59.61
3054	C	MET	639	26.567	14.451	28.934	1.00	60.92
3055	O	MET	639	27.074	14.783	30.000	1.00	59.57
3056	N	TYR	640	27.244	14.409	27.782	1.00	60.93
3057	CA	TYR	640	28.622	14.866	27.693	1.00	62.32
3058	CB	TYR	640	29.585	13.827	27.110	1.00	61.41
3059	CG	TYR	640	30.961	14.446	26.910	1.00	62.45
3060	CD1	TYR	640	31.797	14.687	28.006	1.00	59.75
3061	CE1	TYR	640	32.996	15.372	27.862	1.00	59.57

3062	CD2	TYR	640	31.376	14.906	25.651	1.00	59.20
3063	CE2	TYR	640	32.578	15.594	25.495	1.00	64.39
3064	CZ	TYR	640	33.381	15.827	26.608	1.00	62.16
3065	OH	TYR	640	34.554	16.542	26.485	1.00	62.68
3066	C	TYR	640	28.650	16.082	26.764	1.00	60.42
3067	O	TYR	640	29.264	17.104	27.075	1.00	62.43
3068	N	ASP	641	27.985	15.960	25.619	1.00	63.11
3069	CA	ASP	641	27.946	17.029	24.617	1.00	64.46
3070	CB	ASP	641	26.821	16.780	23.617	1.00	64.30
3071	CG	ASP	641	27.232	17.039	22.196	1.00	61.31
3072	OD1	ASP	641	26.317	17.192	21.353	1.00	59.56
3073	OD2	ASP	641	28.453	17.079	21.917	1.00	63.20
3074	C	ASP	641	27.729	18.401	25.222	1.00	61.02
3075	O	ASP	641	28.073	19.417	24.617	1.00	60.07
3076	N	GLN	642	27.124	18.417	26.406	1.00	63.30
3077	CA	GLN	642	26.801	19.653	27.115	1.00	60.83
3078	CB	GLN	642	25.298	19.837	27.180	1.00	63.77
3079	CG	GLN	642	24.570	18.590	26.781	1.00	59.93
3080	CD	GLN	642	24.905	18.192	25.345	1.00	61.47
3081	OE1	GLN	642	24.656	17.063	24.922	1.00	59.50
3082	NE2	GLN	642	25.462	19.135	24.580	1.00	60.78
3083	C	GLN	642	27.353	19.664	28.518	1.00	60.90
3084	O	GLN	642	27.430	20.714	29.136	1.00	60.17
3085	N	CYS	643	27.678	18.497	29.052	1.00	61.78
3086	CA	CYS	643	28.291	18.491	30.362	1.00	62.44
3087	CB	CYS	643	28.348	17.080	30.963	1.00	66.84
3088	SG	CYS	643	27.004	16.704	32.130	1.00	64.90
3089	C	CYS	643	29.691	18.976	30.015	1.00	61.39
3090	O	CYS	643	30.377	19.587	30.836	1.00	61.37
3091	N	LYS	644	30.093	18.726	28.768	1.00	63.75
3092	CA	LYS	644	31.415	19.128	28.308	1.00	59.22
3093	CB	LYS	644	31.708	18.603	26.889	1.00	57.84
3094	CG	LYS	644	31.163	19.462	25.740	1.00	63.56
3095	CD	LYS	644	31.637	18.994	24.350	1.00	63.09
3096	CE	LYS	644	33.034	19.520	23.983	1.00	63.23
3097	NZ	LYS	644	34.141	19.025	24.872	1.00	61.68
3098	C	LYS	644	31.560	20.641	28.319	1.00	61.63
3099	O	LYS	644	32.672	21.157	28.379	1.00	62.21
3100	N	HIS	645	30.444	21.359	28.267	1.00	59.46
3101	CA	HIS	645	30.518	22.809	28.261	1.00	61.40
3102	CB	HIS	645	29.338	23.380	27.490	1.00	62.01
3103	CG	HIS	645	29.548	23.365	26.009	1.00	61.11
3104	CD2	HIS	645	30.591	23.797	25.261	1.00	62.23
3105	ND1	HIS	645	28.628	22.845	25.123	1.00	62.89
3106	CE1	HIS	645	29.097	22.957	23.892	1.00	60.35
3107	NE2	HIS	645	30.285	23.532	23.948	1.00	58.72
3108	C	HIS	645	30.626	23.413	29.652	1.00	60.22
3109	O	HIS	645	31.097	24.535	29.804	1.00	62.73

3110	N	MET	646	30.205	22.672	30.668	1.00	61.99
3111	CA	MET	646	30.320	23.173	32.027	1.00	60.02
3112	CB	MET	646	29.235	22.574	32.963	1.00	60.39
3113	CG	MET	646	27.846	22.502	32.348	1.00	59.13
3114	SD	MET	646	26.508	21.807	33.298	1.00	59.17
3115	CE	MET	646	25.617	21.251	31.946	1.00	56.97
3116	C	MET	646	31.712	22.761	32.539	1.00	61.22
3117	O	MET	646	32.329	23.495	33.304	1.00	59.33
3118	N	LEU	647	32.207	21.597	32.110	1.00	61.22
3119	CA	LEU	647	33.539	21.146	32.526	1.00	59.88
3120	CB	LEU	647	33.858	19.754	31.962	1.00	64.23
3121	CG	LEU	647	33.205	18.494	32.529	1.00	60.79
3122	CD1	LEU	647	33.267	17.423	31.475	1.00	61.72
3123	CD2	LEU	647	33.901	18.030	33.803	1.00	62.44
3124	C	LEU	647	34.571	22.141	31.997	1.00	62.52
3125	O	LEU	647	35.664	22.292	32.558	1.00	59.55
3126	N	TYR	648	34.220	22.816	30.907	1.00	61.57
3127	CA	TYR	648	35.126	23.785	30.320	1.00	63.01
3128	CB	TYR	648	34.597	24.318	28.997	1.00	64.69
3129	CG	TYR	648	35.477	25.427	28.499	1.00	60.08
3130	CD1	TYR	648	36.741	25.148	27.989	1.00	62.71
3131	CE1	TYR	648	37.617	26.170	27.642	1.00	56.16
3132	CD2	TYR	648	35.104	26.764	28.646	1.00	65.58
3133	CE2	TYR	648	35.974	27.795	28.305	1.00	64.32
3134	CZ	TYR	648	37.226	27.490	27.806	1.00	62.44
3135	OH	TYR	648	38.097	28.500	27.480	1.00	58.63
3136	C	TYR	648	35.380	24.969	31.241	1.00	60.50
3137	O	TYR	648	36.510	25.423	31.369	1.00	59.77
3138	N	VAL	649	34.331	25.490	31.865	1.00	61.19
3139	CA	VAL	649	34.521	26.625	32.754	1.00	62.10
3140	CB	VAL	649	33.164	27.231	33.257	1.00	63.18
3141	CG1	VAL	649	32.254	27.546	32.089	1.00	60.09
3142	CG2	VAL	649	32.476	26.282	34.202	1.00	59.25
3143	C	VAL	649	35.313	26.111	33.941	1.00	63.47
3144	O	VAL	649	36.188	26.791	34.465	1.00	58.78
3145	N	SER	650	35.010	24.884	34.340	1.00	61.57
3146	CA	SER	650	35.664	24.258	35.471	1.00	62.45
3147	CB	SER	650	35.032	22.901	35.727	1.00	63.87
3148	OG	SER	650	35.312	22.468	37.037	1.00	57.30
3149	C	SER	650	37.152	24.102	35.217	1.00	61.59
3150	O	SER	650	37.966	24.254	36.123	1.00	59.77
3151	N	SER	651	37.506	23.796	33.977	1.00	61.81
3152	CA	SER	651	38.904	23.629	33.615	1.00	59.44
3153	CB	SER	651	39.029	23.147	32.175	1.00	61.10
3154	OG	SER	651	40.285	23.527	31.635	1.00	62.25
3155	C	SER	651	39.638	24.942	33.755	1.00	62.21
3156	O	SER	651	40.736	24.994	34.299	1.00	59.39
3157	N	GLU	652	39.019	25.998	33.248	1.00	60.68

3158	CA	GLU	652	39.590	27.333	33.296	1.00	62.47
3159	CB	GLU	652	38.683	28.294	32.534	1.00	62.00
3160	CG	GLU	652	38.551	27.905	31.087	1.00	60.93
3161	CD	GLU	652	39.896	27.841	30.412	1.00	62.60
3162	OE1	GLU	652	40.389	28.912	29.994	1.00	61.37
3163	OE2	GLU	652	40.466	26.727	30.323	1.00	62.86
3164	C	GLU	652	39.803	27.829	34.719	1.00	59.21
3165	O	GLU	652	40.843	28.404	35.040	1.00	60.26
3166	N	LEU	653	38.812	27.613	35.573	1.00	62.17
3167	CA	LEU	653	38.939	28.039	36.949	1.00	61.29
3168	CB	LEU	653	37.630	27.816	37.702	1.00	62.27
3169	CG	LEU	653	36.539	28.833	37.355	1.00	63.87
3170	CD1	LEU	653	35.239	28.428	38.009	1.00	60.88
3171	CD2	LEU	653	36.969	30.220	37.805	1.00	66.93
3172	C	LEU	653	40.065	27.252	37.579	1.00	61.64
3173	O	LEU	653	40.705	27.711	38.526	1.00	62.53
3174	N	HIS	654	40.316	26.067	37.035	1.00	59.14
3175	CA	HIS	654	41.386	25.219	37.534	1.00	63.27
3176	CB	HIS	654	41.122	23.768	37.166	1.00	63.36
3177	CG	HIS	654	42.203	22.842	37.610	1.00	63.44
3178	CD2	HIS	654	43.298	22.379	36.965	1.00	60.81
3179	ND1	HIS	654	42.281	22.360	38.898	1.00	62.60
3180	CE1	HIS	654	43.382	21.642	39.027	1.00	56.60
3181	NE2	HIS	654	44.017	21.639	37.870	1.00	63.72
3182	C	HIS	654	42.719	25.654	36.928	1.00	61.86
3183	O	HIS	654	43.691	25.906	37.636	1.00	63.73
3184	N	ARG	655	42.744	25.732	35.605	1.00	62.82
3185	CA	ARG	655	43.929	26.133	34.867	1.00	60.68
3186	CB	ARG	655	43.559	26.326	33.394	1.00	56.53
3187	CG	ARG	655	44.577	27.074	32.574	1.00	62.54
3188	CD	ARG	655	43.921	27.870	31.451	1.00	58.99
3189	NE	ARG	655	44.865	28.859	30.951	1.00	62.01
3190	CZ	ARG	655	46.081	28.544	30.503	1.00	59.65
3191	NH1	ARG	655	46.475	27.269	30.488	1.00	58.86
3192	NH2	ARG	655	46.926	29.491	30.103	1.00	59.91
3193	C	ARG	655	44.525	27.419	35.430	1.00	59.56
3194	O	ARG	655	45.741	27.524	35.595	1.00	60.27
3195	N	LEU	656	43.664	28.389	35.735	1.00	64.27
3196	CA	LEU	656	44.102	29.687	36.250	1.00	58.78
3197	CB	LEU	656	43.099	30.751	35.833	1.00	62.45
3198	CG	LEU	656	43.072	30.957	34.328	1.00	57.52
3199	CD1	LEU	656	41.832	31.704	33.943	1.00	65.67
3200	CD2	LEU	656	44.305	31.714	33.895	1.00	62.85
3201	C	LEU	656	44.340	29.761	37.757	1.00	61.09
3202	O	LEU	656	44.995	30.688	38.244	1.00	62.48
3203	N	GLN	657	43.816	28.783	38.489	1.00	59.08
3204	CA	GLN	657	43.979	28.736	39.936	1.00	63.09
3205	CB	GLN	657	45.469	28.663	40.307	1.00	58.16

3206	CG	GLN	657	46.052	27.250	40.286	1.00	63.46
3207	CD	GLN	657	45.307	26.310	41.225	1.00	59.61
3208	OE1	GLN	657	44.607	25.392	40.785	1.00	64.27
3209	NE2	GLN	657	45.442	26.547	42.529	1.00	59.12
3210	C	GLN	657	43.335	29.932	40.611	1.00	59.19
3211	O	GLN	657	43.926	30.539	41.498	1.00	61.22
3212	N	VAL	658	42.113	30.249	40.192	1.00	61.76
3213	CA	VAL	658	41.355	31.376	40.734	1.00	61.31
3214	CB	VAL	658	39.970	31.503	40.043	1.00	60.50
3215	CG1	VAL	658	39.211	32.664	40.623	1.00	59.45
3216	CG2	VAL	658	40.132	31.716	38.559	1.00	61.37
3217	C	VAL	658	41.115	31.283	42.240	1.00	58.30
3218	O	VAL	658	40.838	30.208	42.764	1.00	56.60
3219	N	SER	659	41.214	32.418	42.928	1.00	60.76
3220	CA	SER	659	40.979	32.465	44.369	1.00	59.93
3221	CB	SER	659	41.873	33.507	45.047	1.00	59.20
3222	OG	SER	659	41.582	34.817	44.608	1.00	62.34
3223	C	SER	659	39.518	32.789	44.656	1.00	62.94
3224	O	SER	659	38.784	33.247	43.780	1.00	58.10
3225	N	TYR	660	39.097	32.563	45.893	1.00	61.68
3226	CA	TYR	660	37.720	32.808	46.250	1.00	62.54
3227	CB	TYR	660	37.481	32.526	47.717	1.00	64.73
3228	CG	TYR	660	36.014	32.432	48.044	1.00	56.73
3229	CD1	TYR	660	35.144	31.742	47.200	1.00	59.62
3230	CE1	TYR	660	33.817	31.568	47.524	1.00	61.29
3231	CD2	TYR	660	35.507	32.957	49.223	1.00	64.06
3232	CE2	TYR	660	34.176	32.789	49.557	1.00	61.23
3233	CZ	TYR	660	33.336	32.085	48.705	1.00	60.34
3234	OH	TYR	660	32.032	31.840	49.064	1.00	61.17
3235	C	TYR	660	37.250	34.204	45.954	1.00	61.20
3236	O	TYR	660	36.162	34.383	45.433	1.00	65.37
3237	N	GLU	661	38.057	35.199	46.290	1.00	61.50
3238	CA	GLU	661	37.657	36.574	46.052	1.00	58.24
3239	CB	GLU	661	38.598	37.523	46.765	1.00	64.85
3240	CG	GLU	661	38.276	37.577	48.225	1.00	61.43
3241	CD	GLU	661	39.283	38.360	48.991	1.00	60.83
3242	OE1	GLU	661	39.961	39.204	48.365	1.00	59.88
3243	OE2	GLU	661	39.387	38.143	50.219	1.00	59.48
3244	C	GLU	661	37.548	36.918	44.591	1.00	58.50
3245	O	GLU	661	36.573	37.536	44.178	1.00	62.37
3246	N	GLU	662	38.529	36.516	43.798	1.00	63.69
3247	CA	GLU	662	38.453	36.784	42.374	1.00	59.27
3248	CB	GLU	662	39.646	36.158	41.657	1.00	57.91
3249	CG	GLU	662	40.974	36.663	42.122	1.00	62.43
3250	CD	GLU	662	42.104	35.948	41.436	1.00	62.15
3251	OE1	GLU	662	41.969	34.732	41.223	1.00	57.52
3252	OE2	GLU	662	43.128	36.585	41.119	1.00	61.99
3253	C	GLU	662	37.138	36.188	41.831	1.00	61.83

3254	O	GLU	662	36.492	36.771	40.963	1.00	63.75
3255	N	TYR	663	36.751	35.031	42.361	1.00	59.76
3256	CA	TYR	663	35.525	34.336	41.962	1.00	62.22
3257	CB	TYR	663	35.439	32.992	42.694	1.00	58.01
3258	CG	TYR	663	34.073	32.342	42.676	1.00	62.53
3259	CD1	TYR	663	33.536	31.831	41.499	1.00	60.26
3260	CE1	TYR	663	32.298	31.201	41.495	1.00	62.40
3261	CD2	TYR	663	33.330	32.212	43.850	1.00	58.63
3262	CE2	TYR	663	32.096	31.590	43.855	1.00	62.25
3263	CZ	TYR	663	31.587	31.084	42.676	1.00	63.25
3264	OH	TYR	663	30.372	30.448	42.682	1.00	62.04
3265	C	TYR	663	34.240	35.125	42.228	1.00	61.08
3266	O	TYR	663	33.429	35.343	41.322	1.00	58.41
3267	N	LEU	664	34.055	35.528	43.480	1.00	60.59
3268	CA	LEU	664	32.876	36.270	43.884	1.00	61.06
3269	CB	LEU	664	32.976	36.618	45.369	1.00	63.96
3270	CG	LEU	664	33.063	35.440	46.343	1.00	63.81
3271	CD1	LEU	664	33.322	35.929	47.750	1.00	60.79
3272	CD2	LEU	664	31.786	34.656	46.283	1.00	58.66
3273	C	LEU	664	32.692	37.539	43.057	1.00	62.83
3274	O	LEU	664	31.558	37.955	42.812	1.00	59.88
3275	N	CYS	665	33.809	38.139	42.632	1.00	59.97
3276	CA	CYS	665	33.805	39.365	41.831	1.00	63.59
3277	CB	CYS	665	35.167	40.043	41.869	1.00	60.16
3278	SG	CYS	665	35.586	40.757	43.441	1.00	62.94
3279	C	CYS	665	33.475	39.091	40.388	1.00	60.01
3280	O	CYS	665	32.794	39.876	39.735	1.00	57.49
3281	N	MET	666	33.997	37.984	39.883	1.00	60.45
3282	CA	MET	666	33.752	37.601	38.510	1.00	61.35
3283	CB	MET	666	34.733	36.517	38.077	1.00	60.05
3284	CG	MET	666	36.156	36.993	37.902	1.00	63.77
3285	SD	MET	666	37.274	35.592	37.856	1.00	59.75
3286	CE	MET	666	37.139	35.071	36.150	1.00	62.17
3287	C	MET	666	32.338	37.078	38.411	1.00	61.52
3288	O	MET	666	31.681	37.255	37.388	1.00	60.47
3289	N	LYS	667	31.869	36.433	39.475	1.00	61.04
3290	CA	LYS	667	30.516	35.898	39.482	1.00	62.69
3291	CB	LYS	667	30.261	35.036	40.726	1.00	61.46
3292	CG	LYS	667	28.966	34.228	40.671	1.00	59.84
3293	CD	LYS	667	28.678	33.497	41.975	1.00	63.25
3294	CE	LYS	667	28.483	34.471	43.123	1.00	59.23
3295	NZ	LYS	667	27.639	33.891	44.192	1.00	61.97
3296	C	LYS	667	29.554	37.066	39.461	1.00	63.05
3297	O	LYS	667	28.459	36.945	38.942	1.00	60.65
3298	N	THR	668	29.981	38.201	40.011	1.00	61.58
3299	CA	THR	668	29.146	39.398	40.061	1.00	60.37
3300	CB	THR	668	29.609	40.357	41.149	1.00	59.81
3301	OG1	THR	668	29.776	39.634	42.370	1.00	59.26

3302	CG2	THR	668	28.588	41.442	41.365	1.00	57.52
3303	C	THR	668	29.174	40.146	38.746	1.00	60.69
3304	O	THR	668	28.184	40.749	38.348	1.00	61.79
3305	N	LEU	669	30.320	40.111	38.076	1.00	58.82
3306	CA	LEU	669	30.479	40.774	36.786	1.00	60.62
3307	CB	LEU	669	31.947	40.863	36.412	1.00	60.70
3308	CG	LEU	669	32.673	41.944	37.192	1.00	61.83
3309	CD1	LEU	669	34.131	41.996	36.761	1.00	63.30
3310	CD2	LEU	669	31.981	43.275	36.953	1.00	62.82
3311	C	LEU	669	29.736	40.028	35.707	1.00	63.57
3312	O	LEU	669	29.574	40.521	34.599	1.00	63.32
3313	N	LEU	670	29.303	38.823	36.034	1.00	62.04
3314	CA	LEU	670	28.558	38.030	35.087	1.00	64.79
3315	CB	LEU	670	28.662	36.542	35.432	1.00	63.41
3316	CG	LEU	670	29.983	35.838	35.078	1.00	62.66
3317	CD1	LEU	670	29.918	34.407	35.554	1.00	61.38
3318	CD2	LEU	670	30.239	35.867	33.580	1.00	61.74
3319	C	LEU	670	27.111	38.495	35.114	1.00	60.65
3320	O	LEU	670	26.405	38.402	34.119	1.00	60.67
3321	N	LEU	671	26.673	39.008	36.257	1.00	60.80
3322	CA	LEU	671	25.308	39.500	36.386	1.00	60.13
3323	CB	LEU	671	24.977	39.756	37.852	1.00	55.83
3324	CG	LEU	671	23.636	40.403	38.198	1.00	59.73
3325	CD1	LEU	671	22.495	39.498	37.819	1.00	58.32
3326	CD2	LEU	671	23.606	40.677	39.673	1.00	59.37
3327	C	LEU	671	25.178	40.804	35.613	1.00	60.50
3328	O	LEU	671	24.076	41.295	35.377	1.00	61.24
3329	N	LEU	672	26.320	41.354	35.219	1.00	59.65
3330	CA	LEU	672	26.355	42.613	34.492	1.00	62.17
3331	CB	LEU	672	27.128	43.650	35.309	1.00	60.10
3332	CG	LEU	672	26.917	43.688	36.822	1.00	65.92
3333	CD1	LEU	672	27.728	44.819	37.407	1.00	60.54
3334	CD2	LEU	672	25.460	43.885	37.148	1.00	58.59
3335	C	LEU	672	27.027	42.456	33.131	1.00	62.29
3336	O	LEU	672	27.489	43.430	32.554	1.00	61.76
3337	N	SER	673	27.070	41.237	32.613	1.00	60.43
3338	CA	SER	673	27.732	40.980	31.342	1.00	60.60
3339	CB	SER	673	28.212	39.538	31.317	1.00	60.81
3340	OG	SER	673	27.281	38.718	31.987	1.00	56.49
3341	C	SER	673	26.949	41.280	30.074	1.00	60.41
3342	O	SER	673	27.542	41.502	29.020	1.00	60.96
3343	N	SER	674	25.625	41.267	30.160	1.00	62.26
3344	CA	SER	674	24.800	41.565	28.995	1.00	62.20
3345	CB	SER	674	24.359	40.281	28.298	1.00	61.34
3346	OG	SER	674	23.730	39.420	29.221	1.00	62.88
3347	C	SER	674	23.581	42.371	29.402	1.00	60.51
3348	O	SER	674	22.904	42.050	30.376	1.00	62.02
3349	N	VAL	675	23.321	43.432	28.653	1.00	61.79

3350	CA	VAL	675	22.190	44.299	28.911	1.00	61.63
3351	CB	VAL	675	22.670	45.712	29.194	1.00	59.56
3352	CG1	VAL	675	23.388	45.748	30.517	1.00	62.21
3353	CG2	VAL	675	23.598	46.164	28.078	1.00	63.23
3354	C	VAL	675	21.325	44.320	27.658	1.00	62.05
3355	O	VAL	675	21.757	43.861	26.603	1.00	62.28
3356	N	PRO	676	20.077	44.817	27.764	1.00	60.51
3357	CD	PRO	676	19.330	45.132	28.991	1.00	63.50
3358	CA	PRO	676	19.191	44.880	26.593	1.00	62.22
3359	CB	PRO	676	17.896	45.494	27.156	1.00	58.53
3360	CG	PRO	676	18.322	46.117	28.488	1.00	60.68
3361	C	PRO	676	19.839	45.746	25.514	1.00	58.14
3362	O	PRO	676	20.824	46.435	25.792	1.00	61.96
3363	N	LYS	677	19.309	45.710	24.293	1.00	60.64
3364	CA	LYS	677	19.906	46.501	23.215	1.00	59.47
3365	CB	LYS	677	19.025	46.521	21.970	1.00	61.69
3366	CG	LYS	677	19.782	46.912	20.707	1.00	61.32
3367	CD	LYS	677	18.832	47.051	19.514	1.00	61.48
3368	CE	LYS	677	19.604	47.129	18.198	1.00	62.13
3369	NZ	LYS	677	20.435	45.908	17.952	1.00	60.25
3370	C	LYS	677	20.145	47.929	23.686	1.00	59.29
3371	O	LYS	677	21.248	48.235	24.158	1.00	63.94
3372	N	ASP	678	19.129	48.796	23.580	1.00	61.98
3373	CA	ASP	678	19.302	50.178	24.028	1.00	61.19
3374	CB	ASP	678	18.178	51.083	23.506	1.00	60.11
3375	CG	ASP	678	18.515	52.582	23.647	1.00	60.40
3376	OD1	ASP	678	18.311	53.325	22.652	1.00	60.21
3377	OD2	ASP	678	18.980	53.011	24.745	1.00	61.19
3378	C	ASP	678	19.395	50.284	25.558	1.00	61.02
3379	O	ASP	678	18.592	50.955	26.210	1.00	61.94
3380	N	GLY	679	20.398	49.604	26.108	1.00	58.42
3381	CA	GLY	679	20.649	49.605	27.534	1.00	56.97
3382	C	GLY	679	19.449	49.444	28.438	1.00	56.85
3383	O	GLY	679	18.362	49.031	28.028	1.00	59.44
3384	N	LEU	680	19.674	49.788	29.696	1.00	63.29
3385	CA	LEU	680	18.655	49.704	30.727	1.00	62.45
3386	CB	LEU	680	19.297	49.181	32.017	1.00	64.86
3387	CG	LEU	680	20.118	47.895	31.832	1.00	59.84
3388	CD1	LEU	680	20.946	47.595	33.068	1.00	59.62
3389	CD2	LEU	680	19.181	46.760	31.543	1.00	61.01
3390	C	LEU	680	18.056	51.090	30.955	1.00	60.58
3391	O	LEU	680	18.433	52.063	30.298	1.00	62.60
3392	N	LYS	681	17.120	51.174	31.888	1.00	62.27
3393	CA	LYS	681	16.486	52.441	32.197	1.00	63.23
3394	CB	LYS	681	15.146	52.211	32.901	1.00	59.95
3395	CG	LYS	681	14.188	51.417	32.034	1.00	60.87
3396	CD	LYS	681	12.837	51.183	32.665	1.00	61.02
3397	CE	LYS	681	12.004	50.295	31.740	1.00	64.07

3398	NZ	LYS	681	10.616	50.060	32.218	1.00	58.77
3399	C	LYS	681	17.414	53.242	33.072	1.00	60.18
3400	O	LYS	681	17.373	54.462	33.069	1.00	63.10
3401	N	SER	682	18.278	52.554	33.802	1.00	60.92
3402	CA	SER	682	19.214	53.240	34.681	1.00	62.50
3403	CB	SER	682	18.953	52.786	36.113	1.00	62.86
3404	OG	SER	682	17.564	52.589	36.296	1.00	61.69
3405	C	SER	682	20.682	52.993	34.272	1.00	58.65
3406	O	SER	682	21.558	52.781	35.120	1.00	60.76
3407	N	GLN	683	20.924	53.053	32.961	1.00	60.04
3408	CA	GLN	683	22.241	52.840	32.348	1.00	61.19
3409	CB	GLN	683	22.156	53.127	30.850	1.00	59.58
3410	CG	GLN	683	23.397	52.757	30.056	1.00	62.33
3411	CD	GLN	683	23.606	51.259	29.955	1.00	62.33
3412	OE1	GLN	683	22.651	50.502	29.759	1.00	62.13
3413	NE2	GLN	683	24.858	50.823	30.065	1.00	61.30
3414	C	GLN	683	23.397	53.655	32.934	1.00	61.70
3415	O	GLN	683	24.561	53.335	32.719	1.00	62.18
3416	N	GLU	684	23.083	54.710	33.666	1.00	64.02
3417	CA	GLU	684	24.117	55.539	34.257	1.00	60.92
3418	CB	GLU	684	23.541	56.904	34.590	1.00	62.70
3419	CG	GLU	684	22.396	56.780	35.574	1.00	62.30
3420	CD	GLU	684	21.884	58.112	36.063	1.00	61.33
3421	OE1	GLU	684	21.260	58.120	37.153	1.00	61.85
3422	OE2	GLU	684	22.092	59.135	35.363	1.00	62.66
3423	C	GLU	684	24.582	54.867	35.534	1.00	61.21
3424	O	GLU	684	25.741	54.979	35.924	1.00	63.65
3425	N	LEU	685	23.659	54.181	36.197	1.00	62.46
3426	CA	LEU	685	23.992	53.487	37.429	1.00	60.48
3427	CB	LEU	685	22.731	53.265	38.269	1.00	62.31
3428	CG	LEU	685	22.992	53.036	39.764	1.00	59.19
3429	CD1	LEU	685	23.700	54.245	40.360	1.00	59.86
3430	CD2	LEU	685	21.684	52.795	40.485	1.00	61.02
3431	C	LEU	685	24.657	52.148	37.086	1.00	61.95
3432	O	LEU	685	25.524	51.662	37.804	1.00	61.31
3433	N	PHE	686	24.264	51.566	35.964	1.00	60.07
3434	CA	PHE	686	24.832	50.302	35.560	1.00	60.10
3435	CB	PHE	686	24.147	49.785	34.311	1.00	61.65
3436	CG	PHE	686	24.500	48.372	33.990	1.00	62.45
3437	CD1	PHE	686	24.148	47.352	34.860	1.00	58.40
3438	CD2	PHE	686	25.204	48.057	32.839	1.00	57.88
3439	CE1	PHE	686	24.493	46.038	34.589	1.00	58.59
3440	CE2	PHE	686	25.558	46.741	32.558	1.00	63.31
3441	CZ	PHE	686	25.201	45.733	33.433	1.00	61.15
3442	C	PHE	686	26.321	50.423	35.287	1.00	61.88
3443	O	PHE	686	27.150	49.890	36.038	1.00	60.58
3444	N	ASP	687	26.657	51.113	34.199	1.00	62.94
3445	CA	ASP	687	28.048	51.291	33.817	1.00	61.00

3446	CB	ASP	687	28.171	52.397	32.776	1.00	59.08
3447	CG	ASP	687	27.327	52.131	31.555	1.00	63.32
3448	OD1	ASP	687	27.089	50.940	31.271	1.00	59.10
3449	OD2	ASP	687	26.914	53.098	30.875	1.00	63.48
3450	C	ASP	687	28.853	51.645	35.051	1.00	60.66
3451	O	ASP	687	29.988	51.203	35.213	1.00	60.12
3452	N	GLU	688	28.238	52.424	35.934	1.00	62.70
3453	CA	GLU	688	28.869	52.872	37.172	1.00	64.06
3454	CB	GLU	688	27.967	53.930	37.803	1.00	59.69
3455	CG	GLU	688	28.530	54.718	38.963	1.00	60.90
3456	CD	GLU	688	27.609	55.883	39.319	1.00	59.61
3457	OE1	GLU	688	27.607	56.905	38.575	1.00	59.94
3458	OE2	GLU	688	26.871	55.765	40.328	1.00	61.24
3459	C	GLU	688	29.137	51.726	38.164	1.00	62.60
3460	O	GLU	688	30.199	51.659	38.784	1.00	62.63
3461	N	ILE	689	28.166	50.833	38.314	1.00	61.42
3462	CA	ILE	689	28.296	49.691	39.207	1.00	64.18
3463	CB	ILE	689	26.919	49.043	39.453	1.00	57.30
3464	CG2	ILE	689	27.080	47.686	40.125	1.00	62.29
3465	CG1	ILE	689	26.055	49.980	40.297	1.00	63.30
3466	CD1	ILE	689	24.668	49.458	40.545	1.00	63.34
3467	C	ILE	689	29.235	48.654	38.590	1.00	62.15
3468	O	ILE	689	30.079	48.071	39.276	1.00	59.58
3469	N	ARG	690	29.083	48.416	37.290	1.00	63.61
3470	CA	ARG	690	29.938	47.455	36.606	1.00	64.65
3471	CB	ARG	690	29.619	47.429	35.111	1.00	61.26
3472	CG	ARG	690	30.319	46.331	34.331	1.00	60.27
3473	CD	ARG	690	29.665	46.159	32.967	1.00	61.69
3474	NE	ARG	690	30.153	44.983	32.247	1.00	64.60
3475	CZ	ARG	690	31.331	44.907	31.640	1.00	64.30
3476	NH1	ARG	690	32.158	45.946	31.657	1.00	61.69
3477	NH2	ARG	690	31.682	43.793	31.015	1.00	61.35
3478	C	ARG	690	31.387	47.863	36.824	1.00	62.11
3479	O	ARG	690	32.208	47.070	37.268	1.00	63.96
3480	N	MET	691	31.690	49.118	36.521	1.00	58.67
3481	CA	MET	691	33.029	49.642	36.689	1.00	62.38
3482	CB	MET	691	33.015	51.144	36.408	1.00	63.73
3483	CG	MET	691	34.366	51.723	36.003	1.00	63.05
3484	SD	MET	691	35.189	50.799	34.661	1.00	60.35
3485	CE	MET	691	36.714	50.382	35.462	1.00	57.09
3486	C	MET	691	33.533	49.367	38.106	1.00	61.62
3487	O	MET	691	34.653	48.907	38.300	1.00	60.31
3488	N	THR	692	32.691	49.633	39.095	1.00	61.56
3489	CA	THR	692	33.053	49.428	40.490	1.00	59.70
3490	CB	THR	692	31.899	49.838	41.404	1.00	61.08
3491	OG1	THR	692	31.493	51.167	41.074	1.00	61.61
3492	CG2	THR	692	32.331	49.794	42.860	1.00	61.81
3493	C	THR	692	33.478	47.997	40.837	1.00	61.92

3494	O	THR	692	34.349	47.799	41.695	1.00	59.04
3495	N	TYR	693	32.850	47.013	40.190	1.00	58.91
3496	CA	TYR	693	33.183	45.605	40.419	1.00	59.83
3497	CB	TYR	693	31.961	44.711	40.241	1.00	59.81
3498	CG	TYR	693	31.053	44.801	41.437	1.00	63.50
3499	CD1	TYR	693	31.565	44.640	42.728	1.00	59.52
3500	CE1	TYR	693	30.757	44.793	43.844	1.00	63.13
3501	CD2	TYR	693	29.703	45.109	41.297	1.00	59.74
3502	CE2	TYR	693	28.892	45.259	42.409	1.00	61.29
3503	CZ	TYR	693	29.428	45.101	43.671	1.00	62.95
3504	OH	TYR	693	28.625	45.264	44.760	1.00	60.97
3505	C	TYR	693	34.310	45.138	39.530	1.00	62.66
3506	O	TYR	693	34.856	44.059	39.732	1.00	60.97
3507	N	ILE	694	34.648	45.955	38.536	1.00	62.91
3508	CA	ILE	694	35.766	45.651	37.661	1.00	60.76
3509	CB	ILE	694	35.726	46.450	36.347	1.00	63.35
3510	CG2	ILE	694	37.057	46.305	35.611	1.00	58.86
3511	CG1	ILE	694	34.570	45.956	35.480	1.00	59.03
3512	CD1	ILE	694	34.524	46.568	34.109	1.00	64.66
3513	C	ILE	694	36.947	46.106	38.496	1.00	59.29
3514	O	ILE	694	37.976	45.450	38.548	1.00	59.81
3515	N	LYS	695	36.788	47.235	39.171	1.00	60.10
3516	CA	LYS	695	37.850	47.718	40.031	1.00	59.42
3517	CB	LYS	695	37.530	49.111	40.577	1.00	62.71
3518	CG	LYS	695	37.525	50.194	39.543	1.00	56.74
3519	CD	LYS	695	37.579	51.556	40.199	1.00	62.01
3520	CE	LYS	695	37.453	52.666	39.170	1.00	62.05
3521	NZ	LYS	695	37.650	54.002	39.778	1.00	58.55
3522	C	LYS	695	37.996	46.741	41.193	1.00	60.49
3523	O	LYS	695	39.071	46.578	41.744	1.00	58.83
3524	N	GLU	696	36.906	46.084	41.559	1.00	58.96
3525	CA	GLU	696	36.924	45.135	42.663	1.00	63.14
3526	CB	GLU	696	35.489	44.813	43.080	1.00	62.85
3527	CG	GLU	696	35.338	44.392	44.513	1.00	61.99
3528	CD	GLU	696	35.888	45.410	45.497	1.00	62.60
3529	OE1	GLU	696	35.609	46.616	45.353	1.00	60.89
3530	OE2	GLU	696	36.596	44.999	46.438	1.00	59.40
3531	C	GLU	696	37.668	43.855	42.273	1.00	63.03
3532	O	GLU	696	38.281	43.198	43.120	1.00	61.00
3533	N	LEU	697	37.605	43.507	40.990	1.00	61.52
3534	CA	LEU	697	38.279	42.324	40.487	1.00	58.74
3535	CB	LEU	697	37.830	42.018	39.057	1.00	58.36
3536	CG	LEU	697	38.438	40.757	38.439	1.00	63.54
3537	CD1	LEU	697	37.948	39.560	39.208	1.00	57.14
3538	CD2	LEU	697	38.058	40.623	36.972	1.00	63.58
3539	C	LEU	697	39.766	42.633	40.499	1.00	60.87
3540	O	LEU	697	40.599	41.748	40.683	1.00	64.34
3541	N	GLY	698	40.087	43.907	40.303	1.00	63.62

3542	CA	GLY	698	41.472	44.331	40.285	1.00	60.55
3543	C	GLY	698	42.053	44.398	41.677	1.00	61.55
3544	O	GLY	698	43.259	44.268	41.877	1.00	58.62
3545	N	LYS	699	41.180	44.621	42.644	1.00	60.41
3546	CA	LYS	699	41.596	44.689	44.027	1.00	61.47
3547	CB	LYS	699	40.437	45.189	44.903	1.00	62.58
3548	CG	LYS	699	40.251	46.712	44.942	1.00	64.44
3549	CD	LYS	699	39.111	47.088	45.889	1.00	59.70
3550	CE	LYS	699	39.375	48.368	46.707	1.00	60.92
3551	NZ	LYS	699	38.986	49.663	46.056	1.00	62.69
3552	C	LYS	699	42.000	43.284	44.447	1.00	64.59
3553	O	LYS	699	43.044	43.077	45.063	1.00	59.56
3554	N	ALA	700	41.161	42.322	44.080	1.00	58.13
3555	CA	ALA	700	41.376	40.927	44.415	1.00	62.66
3556	CB	ALA	700	40.219	40.103	43.908	1.00	59.89
3557	C	ALA	700	42.678	40.387	43.861	1.00	60.42
3558	O	ALA	700	43.430	39.743	44.577	1.00	61.59
3559	N	ILE	701	42.937	40.662	42.585	1.00	60.42
3560	CA	ILE	701	44.141	40.201	41.898	1.00	63.95
3561	CB	ILE	701	44.105	40.611	40.416	1.00	61.37
3562	CG2	ILE	701	45.396	40.224	39.742	1.00	65.93
3563	CG1	ILE	701	42.921	39.939	39.717	1.00	60.90
3564	CD1	ILE	701	42.697	40.405	38.275	1.00	59.90
3565	C	ILE	701	45.465	40.675	42.514	1.00	61.05
3566	O	ILE	701	46.455	39.931	42.518	1.00	62.71
3567	N	VAL	702	45.495	41.901	43.030	1.00	64.20
3568	CA	VAL	702	46.723	42.409	43.637	1.00	61.51
3569	CB	VAL	702	46.690	43.949	43.841	1.00	61.28
3570	CG1	VAL	702	46.285	44.645	42.546	1.00	61.75
3571	CG2	VAL	702	45.753	44.305	44.983	1.00	63.42
3572	C	VAL	702	46.964	41.753	44.995	1.00	62.93
3573	O	VAL	702	48.101	41.598	45.432	1.00	62.05
3574	N	LYS	703	45.894	41.357	45.665	1.00	61.37
3575	CA	LYS	703	46.057	40.741	46.967	1.00	62.89
3576	CB	LYS	703	44.714	40.683	47.705	1.00	58.24
3577	CG	LYS	703	44.851	40.816	49.215	1.00	61.67
3578	CD	LYS	703	45.460	39.557	49.830	1.00	63.57
3579	CE	LYS	703	46.410	39.869	50.986	1.00	57.61
3580	NZ	LYS	703	46.656	38.664	51.838	1.00	61.16
3581	C	LYS	703	46.645	39.355	46.776	1.00	60.39
3582	O	LYS	703	46.974	38.668	47.731	1.00	61.26
3583	N	ARG	704	46.790	38.951	45.523	1.00	62.02
3584	CA	ARG	704	47.369	37.649	45.214	1.00	61.58
3585	CB	ARG	704	46.408	36.817	44.368	1.00	61.15
3586	CG	ARG	704	45.272	36.177	45.112	1.00	66.70
3587	CD	ARG	704	44.871	34.956	44.350	1.00	62.98
3588	NE	ARG	704	45.731	34.788	43.185	1.00	58.04
3589	CZ	ARG	704	45.973	33.619	42.601	1.00	65.26

3590	NH1	ARG	704	45.422	32.513	43.080	1.00	60.05
3591	NH2	ARG	704	46.761	33.552	41.538	1.00	60.69
3592	C	ARG	704	48.686	37.792	44.445	1.00	62.07
3593	O	ARG	704	49.779	37.725	45.029	1.00	60.23
3594	N	GLU	705	48.555	37.997	43.130	1.00	61.20
3595	CA	GLU	705	49.686	38.134	42.212	1.00	61.45
3596	CB	GLU	705	49.179	38.271	40.776	1.00	59.83
3597	CG	GLU	705	49.038	36.941	40.015	1.00	61.58
3598	CD	GLU	705	48.539	35.764	40.875	1.00	62.88
3599	OE1	GLU	705	47.511	35.908	41.595	1.00	61.37
3600	OE2	GLU	705	49.181	34.685	40.806	1.00	62.83
3601	C	GLU	705	50.601	39.296	42.542	1.00	60.29
3602	O	GLU	705	50.212	40.468	42.446	1.00	61.23
3603	N	GLY	706	51.832	38.935	42.896	1.00	60.12
3604	CA	GLY	706	52.855	39.883	43.288	1.00	62.85
3605	C	GLY	706	53.083	41.191	42.556	1.00	58.46
3606	O	GLY	706	52.603	42.244	42.991	1.00	60.65
3607	N	ASN	707	53.818	41.141	41.449	1.00	62.51
3608	CA	ASN	707	54.158	42.366	40.729	1.00	63.30
3609	CB	ASN	707	55.516	42.196	40.013	1.00	60.74
3610	CG	ASN	707	55.676	40.835	39.356	1.00	60.19
3611	OD1	ASN	707	55.354	39.797	39.950	1.00	59.76
3612	ND2	ASN	707	56.195	40.833	38.128	1.00	59.34
3613	C	ASN	707	53.134	42.993	39.792	1.00	59.87
3614	O	ASN	707	52.054	42.451	39.569	1.00	63.44
3615	N	SER	708	53.501	44.161	39.265	1.00	60.90
3616	CA	SER	708	52.647	44.950	38.382	1.00	58.16
3617	CB	SER	708	53.218	46.366	38.244	1.00	62.09
3618	OG	SER	708	53.403	46.974	39.516	1.00	61.85
3619	C	SER	708	52.432	44.354	36.998	1.00	61.28
3620	O	SER	708	51.400	44.607	36.372	1.00	58.94
3621	N	SER	709	53.393	43.567	36.516	1.00	61.19
3622	CA	SER	709	53.266	42.952	35.193	1.00	59.82
3623	CB	SER	709	54.650	42.527	34.665	1.00	62.14
3624	OG	SER	709	54.658	42.353	33.249	1.00	61.67
3625	C	SER	709	52.338	41.743	35.318	1.00	59.05
3626	O	SER	709	51.508	41.479	34.442	1.00	63.30
3627	N	GLN	710	52.481	41.022	36.426	1.00	63.44
3628	CA	GLN	710	51.652	39.851	36.691	1.00	59.41
3629	CB	GLN	710	52.289	39.036	37.833	1.00	63.27
3630	CG	GLN	710	53.572	38.329	37.354	1.00	60.06
3631	CD	GLN	710	54.362	37.611	38.453	1.00	57.38
3632	OE1	GLN	710	53.781	37.012	39.369	1.00	60.97
3633	NE2	GLN	710	55.701	37.647	38.348	1.00	63.13
3634	C	GLN	710	50.209	40.281	37.010	1.00	62.98
3635	O	GLN	710	49.250	39.584	36.667	1.00	61.41
3636	N	ASN	711	50.087	41.451	37.641	1.00	59.07
3637	CA	ASN	711	48.815	42.048	38.017	1.00	59.32

3638	CB	ASN	711	49.053	43.439	38.610	1.00	62.53
3639	CG	ASN	711	49.400	43.398	40.096	1.00	65.70
3640	OD1	ASN	711	49.886	44.388	40.663	1.00	59.52
3641	ND2	ASN	711	49.140	42.259	40.736	1.00	62.62
3642	C	ASN	711	47.918	42.167	36.792	1.00	61.19
3643	O	ASN	711	46.796	41.644	36.778	1.00	59.41
3644	N	TRP	712	48.418	42.850	35.762	1.00	60.32
3645	CA	TRP	712	47.660	43.044	34.534	1.00	65.58
3646	CB	TRP	712	48.270	44.168	33.711	1.00	59.75
3647	CG	TRP	712	48.272	45.426	34.444	1.00	58.80
3648	CD2	TRP	712	47.148	46.271	34.668	1.00	64.37
3649	CE2	TRP	712	47.577	47.322	35.506	1.00	59.23
3650	CE3	TRP	712	45.812	46.240	34.245	1.00	62.90
3651	CD1	TRP	712	49.313	45.976	35.124	1.00	62.87
3652	NE1	TRP	712	48.905	47.118	35.770	1.00	62.24
3653	CZ2	TRP	712	46.719	48.335	35.935	1.00	60.25
3654	CZ3	TRP	712	44.954	47.247	34.672	1.00	61.54
3655	CH2	TRP	712	45.413	48.281	35.511	1.00	58.28
3656	C	TRP	712	47.538	41.811	33.663	1.00	61.45
3657	O	TRP	712	46.531	41.623	32.992	1.00	63.89
3658	N	GLN	713	48.561	40.974	33.646	1.00	62.44
3659	CA	GLN	713	48.493	39.778	32.823	1.00	60.84
3660	CB	GLN	713	49.865	39.088	32.761	1.00	59.49
3661	CG	GLN	713	50.495	39.114	31.371	1.00	61.40
3662	CD	GLN	713	49.624	38.414	30.336	1.00	60.98
3663	OE1	GLN	713	49.306	38.980	29.285	1.00	60.97
3664	NE2	GLN	713	49.232	37.173	30.629	1.00	62.19
3665	C	GLN	713	47.446	38.847	33.420	1.00	64.17
3666	O	GLN	713	46.843	38.037	32.722	1.00	62.77
3667	N	ARG	714	47.242	38.993	34.724	1.00	60.50
3668	CA	ARG	714	46.276	38.203	35.481	1.00	60.81
3669	CB	ARG	714	46.560	38.352	36.978	1.00	61.22
3670	CG	ARG	714	45.609	37.613	37.897	1.00	60.90
3671	CD	ARG	714	45.858	36.130	37.894	1.00	60.47
3672	NE	ARG	714	44.999	35.455	38.858	1.00	60.72
3673	CZ	ARG	714	44.777	34.145	38.860	1.00	62.42
3674	NH1	ARG	714	45.358	33.382	37.943	1.00	57.63
3675	NH2	ARG	714	43.967	33.601	39.762	1.00	61.24
3676	C	ARG	714	44.877	38.722	35.174	1.00	61.77
3677	O	ARG	714	43.930	37.949	35.007	1.00	61.51
3678	N	PHE	715	44.765	40.044	35.107	1.00	59.93
3679	CA	PHE	715	43.502	40.691	34.809	1.00	62.80
3680	CB	PHE	715	43.630	42.203	34.932	1.00	61.91
3681	CG	PHE	715	42.335	42.909	34.749	1.00	63.38
3682	CD1	PHE	715	41.340	42.779	35.706	1.00	62.36
3683	CD2	PHE	715	42.062	43.610	33.581	1.00	62.07
3684	CE1	PHE	715	40.091	43.323	35.504	1.00	60.49
3685	CE2	PHE	715	40.815	44.162	33.365	1.00	62.56

3686	CZ	PHE	715	39.823	44.017	34.328	1.00	61.44
3687	C	PHE	715	43.046	40.353	33.395	1.00	60.17
3688	O	PHE	715	41.849	40.288	33.115	1.00	59.69
3689	N	TYR	716	44.017	40.157	32.507	1.00	61.56
3690	CA	TYR	716	43.749	39.820	31.116	1.00	60.99
3691	CB	TYR	716	45.043	39.870	30.297	1.00	62.72
3692	CG	TYR	716	44.810	39.609	28.828	1.00	61.29
3693	CD1	TYR	716	44.115	40.530	28.047	1.00	57.90
3694	CE1	TYR	716	43.790	40.253	26.728	1.00	62.63
3695	CD2	TYR	716	45.188	38.399	28.242	1.00	65.06
3696	CE2	TYR	716	44.866	38.111	26.923	1.00	60.30
3697	CZ	TYR	716	44.161	39.044	26.172	1.00	62.23
3698	OH	TYR	716	43.798	38.768	24.870	1.00	58.39
3699	C	TYR	716	43.157	38.419	31.036	1.00	62.09
3700	O	TYR	716	42.085	38.213	30.469	1.00	60.05
3701	N	GLN	717	43.875	37.460	31.611	1.00	62.41
3702	CA	GLN	717	43.449	36.071	31.623	1.00	60.55
3703	CB	GLN	717	44.409	35.222	32.465	1.00	59.06
3704	CG	GLN	717	45.855	35.166	31.978	1.00	60.27
3705	CD	GLN	717	46.758	34.357	32.919	1.00	60.87
3706	OE1	GLN	717	46.844	34.639	34.124	1.00	61.07
3707	NE2	GLN	717	47.437	33.352	32.369	1.00	62.22
3708	C	GLN	717	42.048	35.931	32.194	1.00	59.73
3709	O	GLN	717	41.156	35.383	31.545	1.00	64.26
3710	N	LEU	718	41.867	36.428	33.415	1.00	58.62
3711	CA	LEU	718	40.582	36.348	34.101	1.00	60.65
3712	CB	LEU	718	40.708	36.899	35.530	1.00	61.42
3713	CG	LEU	718	41.661	36.158	36.487	1.00	61.76
3714	CD1	LEU	718	41.717	36.889	37.809	1.00	60.77
3715	CD2	LEU	718	41.210	34.721	36.701	1.00	59.74
3716	C	LEU	718	39.427	37.034	33.375	1.00	59.70
3717	O	LEU	718	38.330	36.495	33.327	1.00	60.84
3718	N	THR	719	39.661	38.211	32.812	1.00	62.09
3719	CA	THR	719	38.608	38.925	32.095	1.00	59.89
3720	CB	THR	719	38.985	40.387	31.900	1.00	63.01
3721	OG1	THR	719	40.248	40.465	31.237	1.00	63.25
3722	CG2	THR	719	39.087	41.082	33.240	1.00	61.82
3723	C	THR	719	38.329	38.291	30.733	1.00	61.35
3724	O	THR	719	37.349	38.622	30.062	1.00	61.10
3725	N	LYS	720	39.203	37.371	30.341	1.00	62.98
3726	CA	LYS	720	39.074	36.651	29.079	1.00	61.71
3727	CB	LYS	720	40.460	36.209	28.588	1.00	62.48
3728	CG	LYS	720	40.500	35.805	27.128	1.00	58.53
3729	CD	LYS	720	40.038	36.972	26.251	1.00	59.89
3730	CE	LYS	720	39.616	36.524	24.842	1.00	58.48
3731	NZ	LYS	720	38.772	37.570	24.209	1.00	60.64
3732	C	LYS	720	38.184	35.430	29.331	1.00	61.74
3733	O	LYS	720	37.479	34.962	28.438	1.00	61.10

3734	N	LEU	721	38.228	34.923	30.560	1.00	61.01
3735	CA	LEU	721	37.417	33.776	30.938	1.00	64.67
3736	CB	LEU	721	37.897	33.187	32.268	1.00	59.87
3737	CG	LEU	721	37.656	31.707	32.594	1.00	61.04
3738	CD1	LEU	721	37.766	31.549	34.095	1.00	57.32
3739	CD2	LEU	721	36.292	31.224	32.130	1.00	59.37
3740	C	LEU	721	35.983	34.277	31.078	1.00	62.25
3741	O	LEU	721	35.031	33.533	30.860	1.00	57.52
3742	N	LEU	722	35.830	35.540	31.455	1.00	62.01
3743	CA	LEU	722	34.503	36.113	31.591	1.00	62.92
3744	CB	LEU	722	34.578	37.497	32.246	1.00	61.91
3745	CG	LEU	722	34.841	37.559	33.754	1.00	58.92
3746	CD1	LEU	722	34.946	38.986	34.193	1.00	62.12
3747	CD2	LEU	722	33.728	36.876	34.507	1.00	62.52
3748	C	LEU	722	33.949	36.226	30.180	1.00	59.20
3749	O	LEU	722	32.883	35.697	29.854	1.00	60.43
3750	N	ASP	723	34.714	36.911	29.344	1.00	60.22
3751	CA	ASP	723	34.379	37.143	27.952	1.00	60.07
3752	CB	ASP	723	35.607	37.697	27.248	1.00	59.74
3753	CG	ASP	723	35.437	39.115	26.832	1.00	60.94
3754	OD1	ASP	723	34.869	39.890	27.626	1.00	63.82
3755	OD2	ASP	723	35.883	39.445	25.713	1.00	63.76
3756	C	ASP	723	33.909	35.899	27.214	1.00	61.21
3757	O	ASP	723	33.108	35.981	26.292	1.00	61.67
3758	N	SER	724	34.414	34.743	27.613	1.00	62.19
3759	CA	SER	724	34.054	33.521	26.923	1.00	62.38
3760	CB	SER	724	35.256	32.578	26.876	1.00	61.26
3761	OG	SER	724	35.743	32.308	28.175	1.00	62.27
3762	C	SER	724	32.869	32.823	27.539	1.00	63.42
3763	O	SER	724	32.419	31.785	27.054	1.00	60.80
3764	N	MET	725	32.352	33.395	28.613	1.00	61.24
3765	CA	MET	725	31.209	32.794	29.265	1.00	60.73
3766	CB	MET	725	30.955	33.461	30.608	1.00	62.85
3767	CG	MET	725	30.460	32.506	31.654	1.00	63.01
3768	SD	MET	725	31.773	31.403	32.092	1.00	57.07
3769	CE	MET	725	30.949	30.380	33.178	1.00	59.44
3770	C	MET	725	30.008	32.987	28.352	1.00	59.13
3771	O	MET	725	29.022	32.254	28.437	1.00	62.11
3772	N	HIS	726	30.105	33.973	27.465	1.00	58.55
3773	CA	HIS	726	29.021	34.267	26.547	1.00	60.99
3774	CB	HIS	726	29.302	35.554	25.769	1.00	62.45
3775	CG	HIS	726	29.036	36.801	26.557	1.00	59.03
3776	CD2	HIS	726	27.909	37.248	27.161	1.00	60.25
3777	ND1	HIS	726	30.003	37.753	26.800	1.00	61.07
3778	CE1	HIS	726	29.484	38.731	27.520	1.00	61.93
3779	NE2	HIS	726	28.215	38.451	27.752	1.00	59.78
3780	C	HIS	726	28.773	33.116	25.601	1.00	58.35
3781	O	HIS	726	27.638	32.696	25.438	1.00	61.58

3782	N	GLU	727	29.816	32.571	24.993	1.00	62.79
3783	CA	GLU	727	29.574	31.461	24.086	1.00	60.53
3784	CB	GLU	727	30.693	31.307	23.055	1.00	59.90
3785	CG	GLU	727	32.005	30.809	23.578	1.00	57.32
3786	CD	GLU	727	32.838	30.187	22.473	1.00	59.99
3787	OE1	GLU	727	34.057	30.013	22.680	1.00	62.44
3788	OE2	GLU	727	32.275	29.862	21.400	1.00	63.27
3789	C	GLU	727	29.351	30.138	24.791	1.00	59.24
3790	O	GLU	727	28.779	29.233	24.203	1.00	62.98
3791	N	VAL	728	29.812	29.992	26.029	1.00	60.19
3792	CA	VAL	728	29.546	28.732	26.721	1.00	58.29
3793	CB	VAL	728	30.493	28.481	27.956	1.00	58.87
3794	CG1	VAL	728	31.261	29.728	28.304	1.00	60.81
3795	CG2	VAL	728	29.694	28.002	29.152	1.00	61.95
3796	C	VAL	728	28.082	28.825	27.145	1.00	59.41
3797	O	VAL	728	27.335	27.848	27.046	1.00	61.38
3798	N	VAL	729	27.670	30.014	27.585	1.00	59.91
3799	CA	VAL	729	26.283	30.238	27.971	1.00	60.73
3800	CB	VAL	729	26.072	31.664	28.504	1.00	63.53
3801	CG1	VAL	729	24.602	32.062	28.406	1.00	62.52
3802	CG2	VAL	729	26.513	31.725	29.946	1.00	62.40
3803	C	VAL	729	25.397	30.004	26.749	1.00	62.11
3804	O	VAL	729	24.279	29.493	26.868	1.00	58.35
3805	N	GLU	730	25.894	30.372	25.571	1.00	59.30
3806	CA	GLU	730	25.133	30.146	24.347	1.00	61.37
3807	CB	GLU	730	25.940	30.546	23.125	1.00	57.56
3808	CG	GLU	730	25.202	31.467	22.199	1.00	61.79
3809	CD	GLU	730	25.875	31.569	20.859	1.00	62.47
3810	OE1	GLU	730	27.039	32.032	20.811	1.00	62.43
3811	OE2	GLU	730	25.235	31.178	19.858	1.00	61.70
3812	C	GLU	730	24.832	28.660	24.267	1.00	60.90
3813	O	GLU	730	23.701	28.244	24.449	1.00	63.19
3814	N	ASN	731	25.864	27.866	24.013	1.00	61.88
3815	CA	ASN	731	25.729	26.416	23.919	1.00	63.18
3816	CB	ASN	731	27.109	25.761	23.859	1.00	56.96
3817	CG	ASN	731	27.516	25.393	22.449	1.00	61.50
3818	OD1	ASN	731	26.909	24.515	21.808	1.00	59.01
3819	ND2	ASN	731	28.552	26.059	21.953	1.00	62.29
3820	C	ASN	731	24.927	25.773	25.045	1.00	62.97
3821	O	ASN	731	24.251	24.772	24.834	1.00	60.93
3822	N	LEU	732	25.002	26.330	26.246	1.00	59.50
3823	CA	LEU	732	24.241	25.737	27.326	1.00	57.74
3824	CB	LEU	732	24.826	26.120	28.668	1.00	61.00
3825	CG	LEU	732	25.964	25.172	29.078	1.00	60.69
3826	CD1	LEU	732	26.278	25.584	30.458	1.00	63.28
3827	CD2	LEU	732	25.589	23.663	29.058	1.00	63.30
3828	C	LEU	732	22.761	26.089	27.240	1.00	61.98
3829	O	LEU	732	21.912	25.269	27.574	1.00	63.87

3830	N	LEU	733	22.456	27.294	26.762	1.00	63.36
3831	CA	LEU	733	21.073	27.744	26.596	1.00	57.15
3832	CB	LEU	733	21.040	29.241	26.290	1.00	60.30
3833	CG	LEU	733	21.134	30.193	27.481	1.00	57.97
3834	CD1	LEU	733	21.471	31.571	26.956	1.00	62.48
3835	CD2	LEU	733	19.824	30.212	28.272	1.00	62.63
3836	C	LEU	733	20.354	26.997	25.470	1.00	63.32
3837	O	LEU	733	19.256	26.475	25.655	1.00	61.30
3838	N	ASN	734	20.965	26.972	24.292	1.00	57.57
3839	CA	ASN	734	20.376	26.285	23.159	1.00	59.44
3840	CB	ASN	734	21.363	26.277	21.994	1.00	57.94
3841	CG	ASN	734	21.671	27.682	21.495	1.00	59.18
3842	OD1	ASN	734	22.072	28.556	22.268	1.00	63.60
3843	ND2	ASN	734	21.476	27.908	20.202	1.00	63.41
3844	C	ASN	734	20.038	24.872	23.594	1.00	60.75
3845	O	ASN	734	18.904	24.423	23.453	1.00	62.53
3846	N	TYR	735	21.017	24.177	24.151	1.00	61.37
3847	CA	TYR	735	20.762	22.823	24.597	1.00	58.79
3848	CB	TYR	735	22.058	22.201	25.158	1.00	58.40
3849	CG	TYR	735	22.087	20.717	24.978	1.00	60.44
3850	CD1	TYR	735	21.309	19.890	25.780	1.00	60.76
3851	CE1	TYR	735	21.240	18.509	25.562	1.00	60.42
3852	CD2	TYR	735	22.815	20.134	23.938	1.00	61.19
3853	CE2	TYR	735	22.750	18.758	23.696	1.00	62.36
3854	CZ	TYR	735	21.961	17.950	24.519	1.00	59.04
3855	OH	TYR	735	21.899	16.583	24.313	1.00	58.73
3856	C	TYR	735	19.649	22.877	25.657	1.00	61.17
3857	O	TYR	735	18.858	21.945	25.790	1.00	63.18
3858	N	CYS	736	19.574	23.995	26.373	1.00	63.51
3859	CA	CYS	736	18.563	24.202	27.403	1.00	65.29
3860	CB	CYS	736	18.922	25.433	28.228	1.00	64.15
3861	SG	CYS	736	17.642	25.957	29.339	1.00	60.76
3862	C	CYS	736	17.183	24.389	26.779	1.00	63.45
3863	O	CYS	736	16.251	23.645	27.090	1.00	61.32
3864	N	PHE	737	17.061	25.391	25.906	1.00	59.77
3865	CA	PHE	737	15.808	25.688	25.209	1.00	61.17
3866	CB	PHE	737	16.014	26.792	24.175	1.00	59.61
3867	CG	PHE	737	16.348	28.129	24.764	1.00	58.80
3868	CD1	PHE	737	16.060	28.414	26.096	1.00	59.85
3869	CD2	PHE	737	16.924	29.119	23.979	1.00	61.58
3870	CE1	PHE	737	16.340	29.669	26.638	1.00	59.75
3871	CE2	PHE	737	17.207	30.374	24.510	1.00	61.15
3872	CZ	PHE	737	16.914	30.649	25.843	1.00	59.90
3873	C	PHE	737	15.280	24.462	24.484	1.00	61.86
3874	O	PHE	737	14.153	24.024	24.714	1.00	64.04
3875	N	GLN	738	16.108	23.932	23.590	1.00	60.57
3876	CA	GLN	738	15.786	22.752	22.798	1.00	61.63
3877	CB	GLN	738	17.078	22.181	22.220	1.00	62.59

3878	CG	GLN	738	16.989	20.805	21.575	1.00	61.50
3879	CD	GLN	738	18.368	20.144	21.521	1.00	62.73
3880	OE1	GLN	738	18.581	19.062	22.093	1.00	60.75
3881	NE2	GLN	738	19.321	20.808	20.853	1.00	61.08
3882	C	GLN	738	15.043	21.677	23.591	1.00	62.87
3883	O	GLN	738	13.970	21.235	23.180	1.00	62.00
3884	N	THR	739	15.595	21.262	24.725	1.00	62.54
3885	CA	THR	739	14.937	20.228	25.513	1.00	62.00
3886	CB	THR	739	15.883	19.572	26.529	1.00	61.40
3887	OG1	THR	739	16.041	20.437	27.659	1.00	59.46
3888	CG2	THR	739	17.234	19.302	25.902	1.00	67.45
3889	C	THR	739	13.721	20.740	26.282	1.00	60.54
3890	O	THR	739	12.911	19.949	26.758	1.00	60.32
3891	N	PHE	740	13.589	22.049	26.433	1.00	60.26
3892	CA	PHE	740	12.426	22.572	27.136	1.00	60.59
3893	CB	PHE	740	12.645	24.013	27.586	1.00	60.53
3894	CG	PHE	740	11.387	24.682	28.073	1.00	60.33
3895	CD1	PHE	740	10.976	24.543	29.399	1.00	60.24
3896	CD2	PHE	740	10.591	25.417	27.196	1.00	60.88
3897	CE1	PHE	740	9.794	25.124	29.842	1.00	62.19
3898	CE2	PHE	740	9.407	26.001	27.629	1.00	63.06
3899	CZ	PHE	740	9.005	25.857	28.954	1.00	59.45
3900	C	PHE	740	11.269	22.562	26.161	1.00	62.20
3901	O	PHE	740	10.102	22.514	26.560	1.00	60.22
3902	N	LEU	741	11.619	22.631	24.877	1.00	61.98
3903	CA	LEU	741	10.650	22.665	23.783	1.00	61.09
3904	CB	LEU	741	11.158	23.561	22.656	1.00	63.24
3905	CG	LEU	741	11.286	25.053	22.919	1.00	57.80
3906	CD1	LEU	741	11.680	25.732	21.617	1.00	59.82
3907	CD2	LEU	741	9.966	25.608	23.455	1.00	59.42
3908	C	LEU	741	10.313	21.316	23.170	1.00	60.22
3909	O	LEU	741	9.748	21.267	22.079	1.00	59.13
3910	N	ASP	742	10.662	20.230	23.845	1.00	61.37
3911	CA	ASP	742	10.388	18.914	23.309	1.00	61.75
3912	CB	ASP	742	11.679	18.315	22.733	1.00	62.29
3913	CG	ASP	742	11.476	16.916	22.145	1.00	59.85
3914	OD1	ASP	742	12.450	16.354	21.576	1.00	62.02
3915	OD2	ASP	742	10.348	16.378	22.253	1.00	63.60
3916	C	ASP	742	9.843	18.041	24.420	1.00	61.37
3917	O	ASP	742	10.614	17.412	25.153	1.00	62.69
3918	N	LYS	743	8.517	18.018	24.564	1.00	61.79
3919	CA	LYS	743	7.882	17.183	25.595	1.00	58.96
3920	CB	LYS	743	6.381	17.501	25.727	1.00	62.19
3921	CG	LYS	743	6.056	18.836	26.404	1.00	57.47
3922	CD	LYS	743	4.545	19.047	26.473	1.00	59.18
3923	CE	LYS	743	4.180	20.313	27.232	1.00	61.36
3924	NZ	LYS	743	2.699	20.507	27.295	1.00	57.73
3925	C	LYS	743	8.055	15.688	25.281	1.00	61.20

3926	O	LYS	743	7.912	14.843	26.165	1.00	60.18
3927	N	THR	744	8.366	15.380	24.020	1.00	59.67
3928	CA	THR	744	8.580	14.007	23.554	1.00	61.15
3929	CB	THR	744	8.792	13.974	22.047	1.00	59.67
3930	OG1	THR	744	7.881	14.890	21.426	1.00	62.19
3931	CG2	THR	744	8.550	12.574	21.513	1.00	63.96
3932	C	THR	744	9.818	13.406	24.202	1.00	61.58
3933	O	THR	744	9.976	12.195	24.261	1.00	62.58
3934	N	MET	745	10.711	14.279	24.646	1.00	57.60
3935	CA	MET	745	11.933	13.887	25.334	1.00	62.60
3936	CB	MET	745	12.982	14.976	25.147	1.00	59.01
3937	CG	MET	745	14.366	14.645	25.612	1.00	60.84
3938	SD	MET	745	15.440	15.948	24.965	1.00	58.90
3939	CE	MET	745	16.317	15.039	23.610	1.00	62.07
3940	C	MET	745	11.435	13.843	26.774	1.00	63.96
3941	O	MET	745	11.973	13.137	27.629	1.00	64.77
3942	N	SER	746	10.394	14.635	27.025	1.00	59.79
3943	CA	SER	746	9.744	14.657	28.326	1.00	60.83
3944	CB	SER	746	9.149	13.249	28.576	1.00	61.05
3945	OG	SER	746	8.512	13.111	29.842	1.00	61.76
3946	C	SER	746	10.597	15.089	29.533	1.00	61.97
3947	O	SER	746	10.576	14.408	30.545	1.00	61.88
3948	N	ILE	747	11.322	16.207	29.443	1.00	60.50
3949	CA	ILE	747	12.140	16.678	30.571	1.00	61.46
3950	CB	ILE	747	13.557	17.115	30.098	1.00	57.79
3951	CG2	ILE	747	14.374	17.635	31.275	1.00	62.83
3952	CG1	ILE	747	14.282	15.911	29.484	1.00	61.46
3953	CD1	ILE	747	15.664	16.211	28.976	1.00	65.11
3954	C	ILE	747	11.441	17.829	31.318	1.00	63.68
3955	O	ILE	747	11.166	18.891	30.747	1.00	62.48
3956	N	GLU	748	11.167	17.597	32.601	1.00	59.16
3957	CA	GLU	748	10.457	18.546	33.466	1.00	62.34
3958	CB	GLU	748	9.803	17.736	34.620	1.00	60.97
3959	CG	GLU	748	8.628	18.410	35.400	1.00	63.60
3960	CD	GLU	748	7.998	17.505	36.516	1.00	59.56
3961	OE1	GLU	748	8.753	16.918	37.340	1.00	61.60
3962	OE2	GLU	748	6.744	17.396	36.574	1.00	62.18
3963	C	GLU	748	11.333	19.701	34.022	1.00	59.89
3964	O	GLU	748	12.503	19.498	34.367	1.00	59.20
3965	N	PHE	749	10.781	20.913	34.046	1.00	62.20
3966	CA	PHE	749	11.484	22.079	34.601	1.00	60.36
3967	CB	PHE	749	11.773	23.202	33.571	1.00	63.43
3968	CG	PHE	749	12.801	22.827	32.506	1.00	62.31
3969	CD1	PHE	749	12.604	21.790	31.624	1.00	63.18
3970	CD2	PHE	749	13.948	23.639	32.305	1.00	58.27
3971	CE1	PHE	749	13.461	21.555	30.545	1.00	59.47
3972	CE2	PHE	749	14.821	23.409	31.221	1.00	59.31
3973	CZ	PHE	749	14.566	22.379	30.341	1.00	60.26

3974	C	PHE	749	10.491	22.634	35.646	1.00	57.34
3975	O	PHE	749	9.296	22.348	35.598	1.00	62.05
3976	N	PRO	750	10.971	23.425	36.612	1.00	61.11
3977	CD	PRO	750	12.322	23.572	37.178	1.00	62.36
3978	CA	PRO	750	9.955	23.918	37.535	1.00	63.79
3979	CB	PRO	750	10.745	24.124	38.834	1.00	59.84
3980	CG	PRO	750	12.072	24.510	38.341	1.00	61.92
3981	C	PRO	750	9.283	25.174	37.042	1.00	61.44
3982	O	PRO	750	9.000	25.325	35.852	1.00	61.38
3983	N	GLU	751	9.016	26.087	37.962	1.00	61.10
3984	CA	GLU	751	8.375	27.335	37.604	1.00	59.57
3985	CB	GLU	751	7.535	27.828	38.778	1.00	60.79
3986	CG	GLU	751	6.534	26.804	39.190	1.00	60.87
3987	CD	GLU	751	5.716	26.358	38.013	1.00	58.45
3988	OE1	GLU	751	6.004	26.825	36.889	1.00	58.76
3989	OE2	GLU	751	4.768	25.564	38.205	1.00	62.99
3990	C	GLU	751	9.449	28.328	37.275	1.00	59.04
3991	O	GLU	751	9.644	28.698	36.115	1.00	63.48
3992	N	MET	752	10.154	28.736	38.319	1.00	62.70
3993	CA	MET	752	11.223	29.693	38.184	1.00	60.75
3994	CB	MET	752	12.241	29.499	39.306	1.00	60.00
3995	CG	MET	752	13.222	30.641	39.392	1.00	60.74
3996	SD	MET	752	12.305	32.203	39.387	1.00	61.02
3997	CE	MET	752	12.040	32.394	41.073	1.00	58.25
3998	C	MET	752	11.919	29.549	36.847	1.00	61.43
3999	O	MET	752	12.062	30.515	36.103	1.00	63.92
4000	N	LEU	753	12.329	28.326	36.537	1.00	61.53
4001	CA	LEU	753	13.044	28.081	35.307	1.00	63.94
4002	CB	LEU	753	13.749	26.729	35.370	1.00	61.07
4003	CG	LEU	753	15.278	26.834	35.432	1.00	59.22
4004	CD1	LEU	753	15.720	27.666	36.636	1.00	60.65
4005	CD2	LEU	753	15.870	25.436	35.488	1.00	56.88
4006	C	LEU	753	12.182	28.179	34.073	1.00	62.24
4007	O	LEU	753	12.539	28.882	33.138	1.00	61.75
4008	N	ALA	754	11.049	27.488	34.061	1.00	58.32
4009	CA	ALA	754	10.156	27.536	32.902	1.00	60.89
4010	CB	ALA	754	8.856	26.790	33.209	1.00	62.87
4011	C	ALA	754	9.851	28.995	32.581	1.00	60.33
4012	O	ALA	754	10.031	29.471	31.454	1.00	61.42
4013	N	GLU	755	9.406	29.698	33.615	1.00	62.19
4014	CA	GLU	755	9.040	31.101	33.535	1.00	60.87
4015	CB	GLU	755	8.481	31.550	34.891	1.00	60.79
4016	CG	GLU	755	7.821	32.911	34.858	1.00	62.93
4017	CD	GLU	755	6.333	32.829	35.097	1.00	56.10
4018	OE1	GLU	755	5.741	31.746	34.841	1.00	59.07
4019	OE2	GLU	755	5.761	33.857	35.531	1.00	65.63
4020	C	GLU	755	10.163	32.053	33.106	1.00	64.44
4021	O	GLU	755	10.006	33.269	33.209	1.00	61.31

4022	N	ILE	756	11.296	31.528	32.653	1.00	60.43
4023	CA	ILE	756	12.382	32.396	32.187	1.00	58.74
4024	CB	ILE	756	13.664	32.292	33.024	1.00	62.34
4025	CG2	ILE	756	14.819	32.942	32.280	1.00	62.52
4026	CG1	ILE	756	13.487	33.000	34.355	1.00	61.56
4027	CD1	ILE	756	14.750	33.012	35.170	1.00	59.91
4028	C	ILE	756	12.725	31.933	30.799	1.00	61.14
4029	O	ILE	756	12.985	32.732	29.904	1.00	61.35
4030	N	ILE	757	12.728	30.618	30.639	1.00	58.95
4031	CA	ILE	757	13.026	30.016	29.362	1.00	60.81
4032	CB	ILE	757	12.990	28.467	29.480	1.00	60.69
4033	CG2	ILE	757	12.522	27.838	28.197	1.00	64.94
4034	CG1	ILE	757	14.378	27.948	29.883	1.00	60.19
4035	CD1	ILE	757	14.463	27.436	31.313	1.00	62.89
4036	C	ILE	757	12.012	30.542	28.348	1.00	59.56
4037	O	ILE	757	12.397	30.991	27.276	1.00	61.79
4038	N	THR	758	10.726	30.521	28.702	1.00	61.66
4039	CA	THR	758	9.677	31.014	27.795	1.00	61.59
4040	CB	THR	758	8.224	30.722	28.323	1.00	63.29
4041	OG1	THR	758	8.188	30.811	29.755	1.00	62.91
4042	CG2	THR	758	7.754	29.343	27.874	1.00	61.73
4043	C	THR	758	9.809	32.516	27.566	1.00	60.10
4044	O	THR	758	9.735	33.002	26.423	1.00	59.44
4045	N	ASN	759	10.023	33.242	28.656	1.00	59.76
4046	CA	ASN	759	10.154	34.691	28.608	1.00	61.77
4047	CB	ASN	759	10.160	35.242	30.034	1.00	62.16
4048	CG	ASN	759	9.352	34.371	30.981	1.00	60.61
4049	OD1	ASN	759	9.601	33.164	31.072	1.00	60.73
4050	ND2	ASN	759	8.379	34.965	31.683	1.00	58.61
4051	C	ASN	759	11.430	35.091	27.886	1.00	63.83
4052	O	ASN	759	11.725	36.278	27.737	1.00	59.18
4053	N	GLN	760	12.191	34.099	27.439	1.00	60.77
4054	CA	GLN	760	13.431	34.395	26.742	1.00	60.74
4055	CB	GLN	760	14.637	34.295	27.690	1.00	63.92
4056	CG	GLN	760	14.546	35.101	28.992	1.00	63.35
4057	CD	GLN	760	15.114	36.508	28.896	1.00	61.91
4058	OE1	GLN	760	16.231	36.714	28.423	1.00	61.24
4059	NE2	GLN	760	14.351	37.482	29.367	1.00	62.64
4060	C	GLN	760	13.687	33.482	25.554	1.00	61.67
4061	O	GLN	760	14.390	33.898	24.631	1.00	58.73
4062	N	ILE	761	13.124	32.264	25.563	1.00	63.30
4063	CA	ILE	761	13.368	31.305	24.476	1.00	62.33
4064	CB	ILE	761	12.102	30.454	24.088	1.00	62.35
4065	CG2	ILE	761	12.345	29.721	22.777	1.00	64.29
4066	CG1	ILE	761	11.834	29.367	25.140	1.00	60.68
4067	CD1	ILE	761	12.794	28.186	25.074	1.00	65.98
4068	C	ILE	761	13.925	32.069	23.273	1.00	60.92
4069	O	ILE	761	15.089	31.875	22.912	1.00	60.54

4070	N	PRO	762	13.128	32.938	22.626	1.00	60.85
4071	CD	PRO	762	11.810	32.652	22.044	1.00	60.12
4072	CA	PRO	762	13.999	33.474	21.571	1.00	60.84
4073	CB	PRO	762	13.355	32.980	20.264	1.00	58.66
4074	CG	PRO	762	12.240	32.017	20.716	1.00	58.17
4075	C	PRO	762	14.222	34.968	21.533	1.00	62.93
4076	O	PRO	762	14.168	35.566	20.457	1.00	59.88
4077	N	LYS	763	14.405	35.599	22.687	1.00	59.58
4078	CA	LYS	763	14.750	37.015	22.653	1.00	62.56
4079	CB	LYS	763	14.713	37.645	24.045	1.00	61.84
4080	CG	LYS	763	15.014	39.141	24.061	1.00	61.96
4081	CD	LYS	763	14.703	39.723	25.430	1.00	62.42
4082	CE	LYS	763	13.428	39.096	25.979	1.00	61.00
4083	NZ	LYS	763	12.992	39.651	27.285	1.00	62.85
4084	C	LYS	763	16.182	36.666	22.292	1.00	58.43
4085	O	LYS	763	16.780	37.217	21.354	1.00	59.83
4086	N	TYR	764	16.668	35.665	23.036	1.00	59.46
4087	CA	TYR	764	17.999	35.106	22.895	1.00	61.50
4088	CB	TYR	764	18.291	34.109	24.020	1.00	62.35
4089	CG	TYR	764	19.085	34.715	25.149	1.00	57.24
4090	CD1	TYR	764	18.526	34.872	26.424	1.00	62.21
4091	CE1	TYR	764	19.236	35.509	27.451	1.00	63.69
4092	CD2	TYR	764	20.378	35.200	24.927	1.00	62.73
4093	CE2	TYR	764	21.095	35.837	25.942	1.00	62.44
4094	CZ	TYR	764	20.516	35.992	27.195	1.00	65.70
4095	OH	TYR	764	21.206	36.670	28.168	1.00	63.44
4096	C	TYR	764	18.156	34.400	21.570	1.00	60.32
4097	O	TYR	764	17.580	34.816	20.556	1.00	60.80
4098	N	SER	765	18.922	33.310	21.597	1.00	62.63
4099	CA	SER	765	19.209	32.535	20.391	1.00	62.57
4100	CB	SER	765	17.908	31.971	19.777	1.00	63.02
4101	OG	SER	765	18.172	31.232	18.586	1.00	63.09
4102	C	SER	765	19.904	33.487	19.403	1.00	61.20
4103	O	SER	765	21.121	33.703	19.474	1.00	60.85
4104	N	ASN	766	19.099	34.064	18.513	1.00	59.31
4105	CA	ASN	766	19.520	35.005	17.477	1.00	61.38
4106	CB	ASN	766	18.344	35.932	17.155	1.00	63.73
4107	CG	ASN	766	17.006	35.195	17.116	1.00	60.04
4108	OD1	ASN	766	16.493	34.720	18.153	1.00	64.69
4109	ND2	ASN	766	16.433	35.091	15.916	1.00	59.73
4110	C	ASN	766	20.764	35.857	17.800	1.00	64.20
4111	O	ASN	766	21.906	35.462	17.491	1.00	60.72
4112	N	GLY	767	20.523	37.032	18.396	1.00	59.36
4113	CA	GLY	767	21.589	37.961	18.766	1.00	63.17
4114	C	GLY	767	21.096	39.388	19.032	1.00	61.77
4115	O	GLY	767	21.905	40.321	19.172	1.00	58.54
4116	N	ASN	768	19.772	39.550	19.118	1.00	61.70
4117	CA	ASN	768	19.115	40.849	19.347	1.00	60.25

4118	CB	ASN	768	17.603	40.673	19.163	1.00	61.86
4119	CG	ASN	768	17.257	39.882	17.898	1.00	63.48
4120	OD1	ASN	768	17.602	38.702	17.772	1.00	58.87
4121	ND2	ASN	768	16.579	40.534	16.956	1.00	59.56
4122	C	ASN	768	19.400	41.566	20.692	1.00	61.21
4123	O	ASN	768	18.781	42.595	20.987	1.00	57.65
4124	N	ILE	769	20.323	41.011	21.490	1.00	60.01
4125	CA	ILE	769	20.764	41.563	22.792	1.00	60.44
4126	CB	ILE	769	20.851	40.456	23.891	1.00	60.23
4127	CG2	ILE	769	21.520	41.004	25.161	1.00	65.73
4128	CG1	ILE	769	19.461	39.920	24.234	1.00	64.63
4129	CD1	ILE	769	19.506	38.773	25.256	1.00	63.56
4130	C	ILE	769	22.197	42.097	22.594	1.00	60.12
4131	O	ILE	769	22.744	41.990	21.495	1.00	59.38
4132	N	LYS	770	22.799	42.660	23.643	1.00	58.87
4133	CA	LYS	770	24.173	43.171	23.568	1.00	63.22
4134	CB	LYS	770	24.210	44.693	23.711	1.00	61.35
4135	CG	LYS	770	25.615	45.304	23.656	1.00	60.38
4136	CD	LYS	770	25.617	46.682	24.324	1.00	59.38
4137	CE	LYS	770	26.765	47.580	23.858	1.00	63.47
4138	NZ	LYS	770	26.704	48.946	24.493	1.00	63.76
4139	C	LYS	770	25.039	42.568	24.665	1.00	59.00
4140	O	LYS	770	24.962	42.967	25.829	1.00	63.74
4141	N	LYS	771	25.868	41.604	24.292	1.00	59.72
4142	CA	LYS	771	26.742	40.984	25.268	1.00	60.78
4143	CB	LYS	771	27.024	39.525	24.871	1.00	59.33
4144	CG	LYS	771	27.854	39.345	23.619	1.00	62.03
4145	CD	LYS	771	28.351	37.906	23.466	1.00	63.82
4146	CE	LYS	771	29.538	37.838	22.501	1.00	59.76
4147	NZ	LYS	771	30.301	36.550	22.571	1.00	57.46
4148	C	LYS	771	28.044	41.798	25.413	1.00	61.42
4149	O	LYS	771	28.800	41.976	24.459	1.00	58.76
4150	N	LEU	772	28.271	42.302	26.623	1.00	61.95
4151	CA	LEU	772	29.444	43.107	26.948	1.00	60.44
4152	CB	LEU	772	29.187	43.864	28.260	1.00	59.38
4153	CG	LEU	772	27.923	44.730	28.267	1.00	63.13
4154	CD1	LEU	772	27.630	45.253	29.656	1.00	60.11
4155	CD2	LEU	772	28.102	45.873	27.289	1.00	62.17
4156	C	LEU	772	30.732	42.272	27.060	1.00	60.10
4157	O	LEU	772	30.764	41.233	27.718	1.00	60.79
4158	N	LEU	773	31.797	42.749	26.423	1.00	61.72
4159	CA	LEU	773	33.074	42.055	26.428	1.00	60.85
4160	CB	LEU	773	33.406	41.580	25.011	1.00	62.82
4161	CG	LEU	773	32.425	40.675	24.265	1.00	63.82
4162	CD1	LEU	773	32.927	40.451	22.866	1.00	60.94
4163	CD2	LEU	773	32.285	39.352	24.966	1.00	62.11
4164	C	LEU	773	34.205	42.942	26.933	1.00	63.04
4165	O	LEU	773	34.271	44.126	26.625	1.00	62.16

4166	N	PHE	774	35.101	42.352	27.712	1.00	60.13
4167	CA	PHE	774	36.246	43.072	28.248	1.00	61.57
4168	CB	PHE	774	36.893	42.279	29.377	1.00	66.09
4169	CG	PHE	774	36.280	42.543	30.698	1.00	61.67
4170	CD1	PHE	774	36.524	43.741	31.355	1.00	59.42
4171	CD2	PHE	774	35.385	41.650	31.248	1.00	56.29
4172	CE1	PHE	774	35.879	44.050	32.536	1.00	64.79
4173	CE2	PHE	774	34.729	41.948	32.435	1.00	61.83
4174	CZ	PHE	774	34.978	43.155	33.080	1.00	62.07
4175	C	PHE	774	37.243	43.261	27.143	1.00	58.09
4176	O	PHE	774	38.081	44.155	27.187	1.00	63.24
4177	N	HIS	775	37.131	42.398	26.143	1.00	61.71
4178	CA	HIS	775	38.022	42.419	25.007	1.00	60.58
4179	CB	HIS	775	39.060	41.319	25.175	1.00	63.99
4180	CG	HIS	775	39.763	41.365	26.492	1.00	62.38
4181	CD2	HIS	775	39.696	40.548	27.567	1.00	61.52
4182	ND1	HIS	775	40.616	42.389	26.838	1.00	62.48
4183	CE1	HIS	775	41.042	42.202	28.074	1.00	59.32
4184	NE2	HIS	775	40.498	41.092	28.538	1.00	62.24
4185	C	HIS	775	37.236	42.196	23.732	1.00	61.77
4186	O	HIS	775	36.461	41.252	23.633	1.00	62.62
4187	N	GLN	776	37.425	43.083	22.765	1.00	58.75
4188	CA	GLN	776	36.759	42.955	21.484	1.00	58.47
4189	CB	GLN	776	36.460	44.340	20.893	1.00	58.08
4190	CG	GLN	776	37.681	45.247	20.680	1.00	63.95
4191	CD	GLN	776	38.236	45.221	19.250	1.00	62.81
4192	OE1	GLN	776	39.158	45.979	18.924	1.00	62.48
4193	NE2	GLN	776	37.680	44.353	18.397	1.00	60.08
4194	C	GLN	776	37.724	42.163	20.599	1.00	60.33
4195	O	GLN	776	37.269	41.235	19.894	1.00	61.93
4196	OXT	GLN	776	38.936	42.474	20.642	1.00	63.26
4197	CB	LYS	741	7.500	39.003	28.905	1.00	62.43
4198	CG	LYS	741	8.600	39.530	28.004	1.00	60.91
4199	CD	LYS	741	9.141	40.875	28.431	1.00	59.52
4200	CE	LYS	741	10.182	41.314	27.418	1.00	62.38
4201	NZ	LYS	741	10.807	42.617	27.779	1.00	64.43
4202	C	LYS	741	6.303	36.975	29.773	1.00	61.31
4203	O	LYS	741	6.054	35.766	29.829	1.00	59.09
4204	N	LYS	741	6.417	37.458	27.272	1.00	62.30
4205	CA	LYS	741	7.109	37.544	28.597	1.00	59.65
4206	N	GLU	742	5.905	37.867	30.689	1.00	62.69
4207	CA	GLU	742	5.163	37.547	31.917	1.00	61.65
4208	CB	GLU	742	4.672	36.083	31.926	1.00	61.06
4209	CG	GLU	742	4.087	35.564	33.257	1.00	61.09
4210	CD	GLU	742	2.705	36.123	33.568	1.00	62.31
4211	OE1	GLU	742	2.138	35.720	34.616	1.00	57.45
4212	OE2	GLU	742	2.195	36.960	32.771	1.00	60.87
4213	C	GLU	742	6.112	37.794	33.099	1.00	63.06

4214	O	GLU	742	5.915	38.741	33.853	1.00	61.76
4215	N	ASN	743	7.151	36.967	33.238	1.00	63.03
4216	CA	ASN	743	8.116	37.101	34.341	1.00	61.82
4217	CB	ASN	743	9.276	38.040	33.958	1.00	58.35
4218	CG	ASN	743	10.217	37.445	32.909	1.00	59.24
4219	OD1	ASN	743	10.071	37.693	31.699	1.00	60.28
4220	ND2	ASN	743	11.198	36.658	33.372	1.00	60.70
4221	C	ASN	743	7.447	37.656	35.604	1.00	61.37
4222	O	ASN	743	8.010	38.522	36.284	1.00	60.15
4223	N	ALA	744	6.245	37.167	35.907	1.00	60.68
4224	CA	ALA	744	5.497	37.626	37.073	1.00	62.31
4225	CB	ALA	744	4.024	37.229	36.940	1.00	62.38
4226	C	ALA	744	6.080	37.067	38.364	1.00	61.35
4227	O	ALA	744	6.168	37.778	39.360	1.00	59.70
4228	N	LEU	745	6.490	35.801	38.346	1.00	61.20
4229	CA	LEU	745	7.062	35.182	39.538	1.00	59.93
4230	CB	LEU	745	7.419	33.710	39.276	1.00	63.15
4231	CG	LEU	745	7.255	32.720	40.448	1.00	63.24
4232	CD1	LEU	745	8.022	31.429	40.158	1.00	59.45
4233	CD2	LEU	745	7.759	33.342	41.745	1.00	59.90
4234	C	LEU	745	8.313	35.934	39.987	1.00	59.41
4235	O	LEU	745	8.520	36.123	41.182	1.00	59.83
4236	N	LEU	746	9.137	36.372	39.031	1.00	63.44
4237	CA	LEU	746	10.375	37.096	39.350	1.00	60.90
4238	CB	LEU	746	11.266	37.239	38.104	1.00	63.43
4239	CG	LEU	746	12.771	36.991	38.300	1.00	64.10
4240	CD1	LEU	746	13.540	37.598	37.140	1.00	61.93
4241	CD2	LEU	746	13.248	37.598	39.612	1.00	58.02
4242	C	LEU	746	10.120	38.485	39.950	1.00	65.26
4243	O	LEU	746	10.649	38.808	41.025	1.00	59.76
4244	N	ARG	747	9.334	39.308	39.255	1.00	61.19
4245	CA	ARG	747	9.012	40.641	39.762	1.00	61.73
4246	CB	ARG	747	7.844	41.256	38.975	1.00	59.04
4247	CG	ARG	747	7.475	42.676	39.421	1.00	57.13
4248	CD	ARG	747	6.596	43.434	38.407	1.00	58.93
4249	NE	ARG	747	7.362	44.324	37.522	1.00	59.01
4250	CZ	ARG	747	7.556	44.118	36.221	1.00	59.60
4251	NH1	ARG	747	7.039	43.043	35.624	1.00	63.96
4252	NH2	ARG	747	8.272	44.987	35.518	1.00	60.37
4253	C	ARG	747	8.651	40.511	41.247	1.00	61.37
4254	O	ARG	747	9.155	41.257	42.090	1.00	62.28
4255	N	TYR	748	7.799	39.541	41.565	1.00	62.06
4256	CA	TYR	748	7.399	39.306	42.941	1.00	60.54
4257	CB	TYR	748	6.517	38.050	43.003	1.00	60.69
4258	CG	TYR	748	6.287	37.521	44.401	1.00	59.67
4259	CD1	TYR	748	7.077	36.488	44.908	1.00	60.21
4260	CE1	TYR	748	6.926	36.044	46.209	1.00	60.77
4261	CD2	TYR	748	5.329	38.093	45.240	1.00	63.30

4262	CE2	TYR	748	5.174	37.654	46.550	1.00	61.08
4263	CZ	TYR	748	5.977	36.631	47.027	1.00	62.49
4264	OH	TYR	748	5.864	36.204	48.331	1.00	59.76
4265	C	TYR	748	8.593	39.190	43.908	1.00	63.27
4266	O	TYR	748	8.702	39.969	44.857	1.00	60.19
4267	N	LEU	749	9.484	38.229	43.663	1.00	62.27
4268	CA	LEU	749	10.661	38.008	44.516	1.00	62.12
4269	CB	LEU	749	11.454	36.792	44.020	1.00	64.20
4270	CG	LEU	749	10.690	35.476	43.873	1.00	58.72
4271	CD1	LEU	749	11.058	34.828	42.554	1.00	61.26
4272	CD2	LEU	749	10.986	34.565	45.039	1.00	61.68
4273	C	LEU	749	11.589	39.223	44.561	1.00	61.27
4274	O	LEU	749	12.241	39.497	45.571	1.00	60.09
4275	N	LEU	750	11.658	39.946	43.455	1.00	60.39
4276	CA	LEU	750	12.503	41.120	43.397	1.00	59.95
4277	CB	LEU	750	12.603	41.607	41.959	1.00	59.67
4278	CG	LEU	750	14.026	41.742	41.404	1.00	65.62
4279	CD1	LEU	750	15.031	40.919	42.205	1.00	61.72
4280	CD2	LEU	750	14.005	41.302	39.953	1.00	61.66
4281	C	LEU	750	11.954	42.216	44.298	1.00	58.16
4282	O	LEU	750	12.712	42.855	45.032	1.00	61.93
4283	N	ASP	751	10.637	42.423	44.242	1.00	60.02
4284	CA	ASP	751	9.969	43.428	45.073	1.00	61.63
4285	CB	ASP	751	8.539	43.658	44.616	1.00	59.82
4286	CG	ASP	751	8.381	44.973	43.912	1.00	60.49
4287	OD1	ASP	751	9.166	45.214	42.968	1.00	59.40
4288	OD2	ASP	751	7.491	45.767	44.298	1.00	59.17
4289	C	ASP	751	9.941	43.037	46.531	1.00	62.48
4290	O	ASP	751	10.367	43.813	47.383	1.00	63.09
4291	N	LYS	752	9.421	41.841	46.808	1.00	64.09
4292	CA	LYS	752	9.346	41.308	48.164	1.00	60.89
4293	CB	LYS	752	9.881	39.882	48.216	1.00	63.21
4294	CG	LYS	752	9.051	38.811	47.568	1.00	57.72
4295	CD	LYS	752	9.168	37.532	48.396	1.00	60.58
4296	CE	LYS	752	8.769	37.801	49.858	1.00	63.26
4297	NZ	LYS	752	8.598	36.571	50.686	1.00	60.07
4298	C	LYS	752	10.218	42.123	49.090	1.00	59.75
4299	O	LYS	752	11.426	42.228	48.869	1.00	61.26
4300	N	ASP	753	9.644	42.700	50.132	1.00	64.75
4301	CA	ASP	753	10.478	43.462	51.039	1.00	60.32
4302	CB	ASP	753	9.643	44.126	52.126	1.00	62.72
4303	CG	ASP	753	10.496	44.762	53.198	1.00	62.87
4304	OD1	ASP	753	11.420	45.549	52.863	1.00	59.14
4305	OD2	ASP	753	10.239	44.468	54.382	1.00	63.19
4306	C	ASP	753	11.455	42.468	51.647	1.00	60.33
4307	O	ASP	753	12.111	42.750	52.646	1.00	61.12
4308	N	ALA	754	11.528	41.304	51.008	1.00	59.93
4309	CA	ALA	754	12.396	40.177	51.356	1.00	61.16

4310	CB	ALA	754	12.896	39.509	50.053	1.00	64.36
4311	C	ALA	754	13.587	40.401	52.307	1.00	59.44
4312	O	ALA	754	14.700	39.937	52.047	1.00	61.71
4313	N	THR	755	13.355	41.108	53.403	1.00	60.67
4314	CA	THR	755	14.375	41.342	54.420	1.00	60.98
4315	CB	THR	755	15.250	42.613	54.137	1.00	63.96
4316	OG1	THR	755	14.460	43.794	54.313	1.00	60.28
4317	CG2	THR	755	15.824	42.582	52.696	1.00	57.43
4318	C	THR	755	13.505	41.499	55.671	1.00	59.27
4319	O	THR	755	13.323	42.586	56.237	1.00	60.51
4320	N	ALA	756	12.918	40.356	56.024	1.00	62.21
4321	CA	ALA	756	12.025	40.165	57.162	1.00	59.83
4322	CB	ALA	756	11.075	38.993	56.870	1.00	60.21
4323	C	ALA	756	12.890	39.842	58.372	1.00	61.08
4324	O	ALA	756	12.461	39.941	59.531	1.00	61.80
4325	N	ALA	757	14.115	39.426	58.072	1.00	62.43
4326	CA	ALA	757	15.087	39.099	59.092	1.00	60.57
4327	CB	ALA	757	16.415	38.753	58.431	1.00	60.81
4328	C	ALA	757	15.211	40.367	59.932	1.00	61.35
4329	O	ALA	757	15.146	41.460	59.327	1.00	62.10
4330	OXT	ALA	757	15.354	40.253	61.169	1.00	58.48
4331	O	HOH	1	62.349	-1.370	59.183	1.00	61.82
4332	O	HOH	2	63.098	9.775	56.010	1.00	63.21
4333	O	HOH	3	29.467	50.468	47.493	1.00	60.82
4334	O	HOH	4	24.799	1.025	51.054	1.00	63.04
4335	O	HOH	5	25.120	35.371	29.890	1.00	58.53
4336	O	HOH	6	62.603	13.819	69.179	1.00	62.10
4337	O	HOH	7	43.394	-0.575	64.086	1.00	61.07
4338	O	HOH	8	33.029	27.080	24.812	1.00	63.53
4339	O	HOH	9	40.476	0.604	50.517	1.00	62.87
4340	O	HOH	10	42.083	33.017	29.431	1.00	59.31
4341	O	HOH	11	40.224	-1.905	63.310	1.00	60.38
4342	O	HOH	12	29.926	49.219	30.317	1.00	60.19
4343	O	HOH	13	63.481	3.211	57.703	1.00	62.93
4344	O	HOH	14	45.679	44.833	38.756	1.00	60.97
4345	O	HOH	15	21.388	1.839	41.400	1.00	61.41
4346	O	HOH	16	47.452	-16.061	63.707	1.00	60.73
4347	O	HOH	17	52.653	15.955	63.901	1.00	64.75
4348	O	HOH	18	62.913	1.964	67.923	1.00	64.33
4349	O	HOH	19	62.507	3.936	69.792	1.00	60.95
4350	O	HOH	20	11.730	26.749	44.436	1.00	60.79
4351	O	HOH	21	48.735	13.308	64.587	1.00	62.06
4352	O	HOH	22	32.377	39.863	58.144	1.00	63.51
4353	O	HOH	23	58.924	9.831	70.947	1.00	61.40
4354	O	HOH	24	39.278	17.448	64.290	1.00	62.12
4355	O	HOH	25	40.573	48.042	36.816	1.00	60.96
4356	O	HOH	26	40.494	35.299	48.387	1.00	59.93
4357	O	HOH	27	61.454	1.678	61.901	1.00	60.51

4358	O	HOH	28	9.075	22.638	42.296	1.00	61.65
4359	O	HOH	29	51.369	13.900	63.592	1.00	64.00
4360	O	HOH	30	61.184	-0.481	44.937	1.00	61.95
4361	O	HOH	31	19.041	16.035	52.737	1.00	60.85
4362	O	HOH	32	37.487	3.963	49.092	1.00	60.40
4363	O	HOH	33	31.183	34.399	55.395	1.00	61.32
4364	O	HOH	34	25.672	33.490	53.795	1.00	61.76
4365	O	HOH	35	24.467	27.177	45.107	1.00	62.37
4366	O	HOH	36	47.899	30.685	35.691	1.00	60.62
4367	O	HOH	37	31.250	45.014	24.427	1.00	63.26
4368	O	HOH	38	60.719	-0.340	49.987	1.00	60.94
4369	O	HOH	39	48.761	14.305	46.147	1.00	59.45
4370	O	HOH	40	52.252	11.824	45.533	1.00	59.86
4371	O	HOH	41	40.704	30.604	47.765	1.00	62.04
4372	O	HOH	42	34.599	19.541	73.265	1.00	61.69
4373	O	HOH	43	44.135	32.951	48.092	1.00	60.11
4374	O	HOH	44	16.447	16.136	55.224	1.00	58.77
4375	O	HOH	45	37.470	21.079	29.057	1.00	61.47
4376	O	HOH	46	14.411	15.785	52.085	1.00	58.97
4377	O	HOH	47	27.199	25.588	51.919	1.00	58.58
4378	O	HOH	48	32.466	25.097	53.254	1.00	60.88
4379	O	HOH	49	17.927	39.612	49.972	1.00	61.48
4380	O	HOH	50	17.243	38.022	52.339	1.00	61.61
4381	O	HOH	51	65.714	6.374	72.458	1.00	61.45
4382	O	HOH	52	25.540	34.686	57.601	1.00	59.81
4383	O	HOH	53	22.812	3.452	38.767	1.00	62.42
4384	C1	DEX	1	31.791	3.330	56.615	1.00	59.00
4385	H1	DEX	1	30.892	2.719	56.626	1.00	59.00
4386	C2	DEX	1	32.066	4.057	55.552	1.00	59.00
4387	H2	DEX	1	31.418	4.016	54.717	1.00	59.00
4388	C3	DEX	1	33.314	4.929	55.514	1.00	59.00
4389	C4	DEX	1	34.176	5.061	56.733	1.00	59.00
4390	H4	DEX	1	35.013	5.729	56.720	1.00	59.00
4391	C5	DEX	1	33.915	4.329	57.855	1.00	59.00
4392	C6	DEX	1	34.782	4.456	59.133	1.00	59.00
4393	H61	DEX	1	35.558	5.172	59.015	1.00	59.00
4394	H62	DEX	1	35.262	3.483	59.339	1.00	59.00
4395	C7	DEX	1	33.905	4.834	60.331	1.00	59.00
4396	H71	DEX	1	33.520	5.861	60.202	1.00	59.00
4397	H72	DEX	1	34.515	4.837	61.236	1.00	59.00
4398	C8	DEX	1	32.690	3.903	60.544	1.00	59.00
4399	H8	DEX	1	33.063	2.878	60.787	1.00	59.00
4400	C9	DEX	1	31.759	3.803	59.162	1.00	59.00
4401	C10	DEX	1	32.677	3.304	57.900	1.00	59.00
4402	C11	DEX	1	30.360	2.986	59.327	1.00	59.00
4403	H11	DEX	1	29.743	3.203	58.478	1.00	59.00
4404	C12	DEX	1	29.599	3.415	60.596	1.00	59.00
4405	H121	DEX	1	28.744	2.788	60.729	1.00	59.00

4406	H122	DEX	1	29.221	4.448	60.436	1.00	59.00
4407	C13	DEX	1	30.518	3.414	61.924	1.00	59.00
4408	C14	DEX	1	31.758	4.387	61.726	1.00	59.00
4409	H14	DEX	1	31.359	5.403	61.401	1.00	59.00
4410	C15	DEX	1	32.374	4.589	63.095	1.00	59.00
4411	H151	DEX	1	32.893	5.547	63.111	1.00	59.00
4412	H152	DEX	1	33.119	3.796	63.281	1.00	59.00
4413	C16	DEX	1	31.175	4.486	64.093	1.00	59.00
4414	H16	DEX	1	31.391	3.605	64.743	1.00	59.00
4415	C17	DEX	1	29.863	4.144	63.168	1.00	59.00
4416	C18	DEX	1	30.929	1.834	62.325	1.00	59.00
4417	H181	DEX	1	31.535	1.833	63.241	1.00	59.00
4418	H182	DEX	1	30.050	1.248	62.496	1.00	59.00
4419	H183	DEX	1	31.537	1.374	61.558	1.00	59.00
4420	C19	DEX	1	33.270	1.833	58.015	1.00	59.00
4421	H191	DEX	1	33.916	1.724	58.905	1.00	59.00
4422	H192	DEX	1	32.485	1.095	58.112	1.00	59.00
4423	H193	DEX	1	33.870	1.605	57.134	1.00	59.00
4424	C20	DEX	1	28.759	3.270	63.873	1.00	59.00
4425	C21	DEX	1	27.338	3.348	63.353	1.00	59.00
4426	H211	DEX	1	27.350	3.637	62.283	1.00	59.00
4427	H212	DEX	1	26.827	4.148	63.876	1.00	59.00
4428	C22	DEX	1	31.008	5.693	64.947	1.00	59.00
4429	H221	DEX	1	30.160	5.560	65.619	1.00	59.00
4430	H222	DEX	1	31.912	5.877	65.542	1.00	59.00
4431	H223	DEX	1	30.811	6.588	64.313	1.00	59.00
4432	F1	DEX	1	31.331	5.130	58.833	1.00	59.00
4433	O1	DEX	1	33.617	5.512	54.507	1.00	59.00
4434	O2	DEX	1	30.601	1.580	59.361	1.00	59.00
4435	HO2	DEX	1	29.784	1.163	59.706	1.00	59.00
4436	O3	DEX	1	29.236	5.409	62.711	1.00	59.00
4437	H3	DEX	1	28.816	5.780	63.475	1.00	59.00
4438	O4	DEX	1	29.058	2.511	64.818	1.00	59.00
4439	O5	DEX	1	26.689	2.117	63.492	1.00	59.00
4440	H5	DEX	1	25.816	2.344	63.756	1.00	59.00
4441	C1	DEX	1	21.344	23.582	37.624	1.00	59.00
4442	H1	DEX	1	20.325	23.208	37.634	1.00	59.00
4443	C2	DEX	1	22.105	23.392	38.670	1.00	59.00
4444	H2	DEX	1	21.710	22.910	39.509	1.00	59.00
4445	C3	DEX	1	23.539	23.892	38.687	1.00	59.00
4446	C4	DEX	1	24.137	24.501	37.450	1.00	59.00
4447	H4	DEX	1	25.173	24.791	37.441	1.00	59.00
4448	C5	DEX	1	23.372	24.700	36.346	1.00	59.00
4449	C6	DEX	1	23.965	25.312	35.061	1.00	59.00
4450	H61	DEX	1	24.996	25.542	35.157	1.00	59.00
4451	H62	DEX	1	23.444	26.267	34.853	1.00	59.00
4452	C7	DEX	1	23.752	24.345	33.877	1.00	59.00
4453	H71	DEX	1	24.370	23.444	34.001	1.00	59.00

4454	H72	DEX	1	24.092	24.829	32.956	1.00	59.00
4455	C8	DEX	1	22.275	23.885	33.692	1.00	59.00
4456	H8	DEX	1	21.638	24.764	33.460	1.00	59.00
4457	C9	DEX	1	21.676	23.232	35.081	1.00	59.00
4458	C10	DEX	1	21.819	24.294	36.329	1.00	59.00
4459	C11	DEX	1	20.197	22.585	34.938	1.00	59.00
4460	H11	DEX	1	20.028	21.974	35.784	1.00	59.00
4461	C12	DEX	1	20.107	21.699	33.700	1.00	59.00
4462	H121	DEX	1	19.130	21.365	33.602	1.00	59.00
4463	H122	DEX	1	20.720	20.795	33.859	1.00	59.00
4464	C13	DEX	1	20.600	22.429	32.344	1.00	59.00
4465	C14	DEX	1	22.105	22.863	32.515	1.00	59.00
4466	H14	DEX	1	22.701	21.953	32.834	1.00	59.00
4467	C15	DEX	1	22.602	23.242	31.129	1.00	59.00
4468	H151	DEX	1	23.685	23.110	31.097	1.00	59.00
4469	H152	DEX	1	22.383	24.310	30.934	1.00	59.00
4470	C16	DEX	1	21.806	22.306	30.152	1.00	59.00
4471	H16	DEX	1	21.207	22.984	29.504	1.00	59.00
4472	C17	DEX	1	20.783	21.450	31.097	1.00	59.00
4473	C18	DEX	1	19.540	23.677	31.944	1.00	59.00
4474	H181	DEX	1	19.873	24.157	31.015	1.00	59.00
4475	H182	DEX	1	18.547	23.297	31.792	1.00	59.00
4476	H183	DEX	1	19.525	24.449	32.700	1.00	59.00
4477	C19	DEX	1	20.959	25.638	36.205	1.00	59.00
4478	H191	DEX	1	21.232	26.215	35.303	1.00	59.00
4479	H192	DEX	1	19.899	25.426	36.127	1.00	59.00
4480	H193	DEX	1	21.132	26.270	37.072	1.00	59.00
4481	C20	DEX	1	19.417	21.067	30.421	1.00	59.00
4482	C21	DEX	1	18.443	20.176	31.204	1.00	59.00
4483	H211	DEX	1	17.932	20.800	31.959	1.00	59.00
4484	H212	DEX	1	19.031	19.423	31.779	1.00	59.00
4485	C22	DEX	1	22.671	21.454	29.301	1.00	59.00
4486	H221	DEX	1	22.061	20.835	28.644	1.00	59.00
4487	H222	DEX	1	23.334	22.077	28.688	1.00	59.00
4488	H223	DEX	1	23.300	20.785	29.933	1.00	59.00
4489	F1	DEX	1	22.519	22.128	35.397	1.00	59.00
4490	O1	DEX	1	24.201	23.808	39.692	1.00	59.00
4491	O2	DEX	1	19.179	23.598	34.905	1.00	59.00
4492	HO2	DEX	1	18.367	23.168	34.580	1.00	59.00
4493	O3	DEX	1	21.444	20.210	31.554	1.00	59.00
4494	H3	DEX	1	21.502	19.648	30.802	1.00	59.00
4495	O4	DEX	1	19.127	21.505	29.299	1.00	59.00
4496	O5	DEX	1	17.530	19.572	30.381	1.00	59.00
4497	H5	DEX	1	17.435	18.711	30.744	1.00	59.00

TABLE 5
ATOMIC COORDINATES FOR THE GR/SRC-1 MODEL USED IN MOLECULAR
REPLACEMENT

ATOM	ATOM TYPE	RESIDUE	PROTEIN #	#	X	Y	Z	OCC
1	N	GLN	527	-10.228	40.054	15.641	1.00	69.36
2	CA	GLN	527	-10.481	38.584	15.329	1.00	66.54
3	C	GLN	527	-9.230	37.821	15.751	1.00	66.47
4	O	GLN	527	-9.189	37.229	16.832	1.00	66.82
5	CB	GLN	527	-10.824	38.264	13.878	1.00	68.47
6	CG	GLN	527	-11.131	36.765	13.555	1.00	99.90
7	CD	GLN	527	-11.424	36.357	12.106	1.00	99.90
8	OE1	GLN	527	-11.629	35.191	11.807	1.00	99.90
9	NE2	GLN	527	-11.432	37.263	11.161	1.00	99.90
10	N	LEU	528	-8.211	37.835	14.896	1.00	63.30
11	CA	LEU	528	-6.966	37.146	15.198	1.00	60.85
12	C	LEU	528	-5.949	38.070	15.865	1.00	56.94
13	O	LEU	528	-5.120	37.612	16.653	1.00	54.60
14	CB	LEU	528	-6.361	36.538	13.925	1.00	61.13
15	CG	LEU	528	-7.168	35.430	13.235	1.00	66.50
16	CD1	LEU	528	-6.400	34.910	12.020	1.00	60.00
17	CD2	LEU	528	-7.426	34.291	14.214	1.00	59.53
18	N	THR	529	-6.012	39.362	15.551	1.00	52.97
19	CA	THR	529	-5.083	40.319	16.141	1.00	48.69
20	C	THR	529	-5.489	40.584	17.589	1.00	46.25
21	O	THR	529	-6.595	41.044	17.853	1.00	41.04
22	CB	THR	529	-5.082	41.664	15.381	1.00	52.18
23	OG1	THR	529	-4.666	41.475	14.034	1.00	99.90
24	CG2	THR	529	-4.139	42.758	15.927	1.00	99.90
25	N	PRO	530	-4.595	40.292	18.548	1.00	40.66
26	CA	PRO	530	-4.883	40.507	19.968	1.00	39.82
27	C	PRO	530	-5.301	41.950	20.272	1.00	36.13
28	O	PRO	530	-4.811	42.889	19.648	1.00	35.64
29	CB	PRO	530	-3.570	40.108	20.640	1.00	34.22
30	CG	PRO	530	-3.073	39.021	19.725	1.00	43.36
31	CD	PRO	530	-3.240	39.737	18.398	1.00	40.38
32	N	THR	531	-6.206	42.135	21.243	1.00	35.29
33	CA	THR	531	-6.722	43.444	21.654	1.00	35.12
34	C	THR	531	-5.642	44.469	21.993	1.00	30.01
35	O	THR	531	-5.687	45.610	21.527	1.00	29.64
36	CB	THR	531	-7.584	43.099	22.866	1.00	36.34
37	OG1	THR	531	-8.643	42.227	22.491	1.00	99.90
38	CG2	THR	531	-8.286	44.282	23.567	1.00	99.90
39	N	LEU	532	-4.676	44.056	22.805	1.00	29.04

40	CA	LEU	532	-3.597	44.958	23.211	1.00	28.23
41	C	LEU	532	-2.763	45.434	22.022	1.00	26.62
42	O	LEU	532	-2.299	46.580	21.984	1.00	25.82
43	CB	LEU	532	-2.702	44.274	24.232	1.00	25.68
44	CG	LEU	532	-1.563	45.146	24.757	1.00	34.63
45	CD1	LEU	532	-2.111	46.509	25.197	1.00	30.55
46	CD2	LEU	532	-0.867	44.418	25.902	1.00	30.65
47	N	VAL	533	-2.571	44.555	21.045	1.00	27.06
48	CA	VAL	533	-1.809	44.925	19.863	1.00	23.18
49	C	VAL	533	-2.593	45.921	19.014	1.00	24.05
50	O	VAL	533	-2.030	46.890	18.496	1.00	26.77
51	CB	VAL	533	-1.442	43.683	19.053	1.00	23.51
52	CG1	VAL	533	-0.483	42.716	19.788	1.00	99.90
53	CG2	VAL	533	-0.787	43.933	17.666	1.00	99.90
54	N	SER	534	-3.900	45.708	18.871	1.00	25.92
55	CA	SER	534	-4.703	46.659	18.103	1.00	27.71
56	C	SER	534	-4.657	48.017	18.811	1.00	22.00
57	O	SER	534	-4.612	49.063	18.165	1.00	26.26
58	CB	SER	534	-6.156	46.179	17.998	1.00	31.49
59	OG	SER	534	-6.853	46.235	19.247	1.00	99.90
60	N	LEU	535	-4.662	48.000	20.140	1.00	26.88
61	CA	LEU	535	-4.620	49.258	20.894	1.00	25.43
62	C	LEU	535	-3.296	49.974	20.628	1.00	27.05
63	O	LEU	535	-3.273	51.177	20.377	1.00	26.07
64	CB	LEU	535	-4.802	48.981	22.385	1.00	26.35
65	CG	LEU	535	-4.863	50.186	23.336	1.00	35.60
66	CD1	LEU	535	-5.553	49.756	24.633	1.00	36.71
67	CD2	LEU	535	-3.464	50.735	23.618	1.00	30.46
68	N	LEU	536	-2.197	49.230	20.652	1.00	25.73
69	CA	LEU	536	-0.883	49.817	20.384	1.00	23.64
70	C	LEU	536	-0.843	50.404	18.977	1.00	27.62
71	O	LEU	536	-0.242	51.450	18.756	1.00	22.81
72	CB	LEU	536	0.221	48.764	20.527	1.00	24.64
73	CG	LEU	536	0.433	48.131	21.906	1.00	25.70
74	CD1	LEU	536	1.559	47.084	21.835	1.00	21.63
75	CD2	LEU	536	0.782	49.226	22.923	1.00	20.83
76	N	GLU	537	-1.455	49.717	18.013	1.00	24.62
77	CA	GLU	537	-1.488	50.230	16.646	1.00	27.60
78	C	GLU	537	-2.257	51.555	16.668	1.00	27.94
79	O	GLU	537	-1.850	52.543	16.060	1.00	25.86
80	CB	GLU	537	-2.207	49.232	15.730	1.00	27.45
81	CG	GLU	537	-2.284	49.639	14.284	1.00	39.52
82	CD	GLU	537	-3.073	48.750	13.320	1.00	99.90
83	OE1	GLU	537	-3.217	49.017	12.134	1.00	99.90
84	OE2	GLU	537	-3.596	47.637	13.905	1.00	99.90
85	N	VAL	538	-3.358	51.575	17.406	1.00	25.24
86	CA	VAL	538	-4.180	52.769	17.476	1.00	31.97
87	C	VAL	538	-3.512	53.961	18.152	1.00	29.88

88	O	VAL	538	-3.776	55.107	17.786	1.00	28.14
89	CB	VAL	538	-5.505	52.468	18.192	1.00	38.05
90	CG1	VAL	538	-6.415	51.472	17.434	1.00	99.90
91	CG2	VAL	538	-6.410	53.691	18.509	1.00	99.90
92	N	ILE	539	-2.649	53.719	19.132	1.00	25.23
93	CA	ILE	539	-2.029	54.861	19.808	1.00	26.22
94	C	ILE	539	-0.676	55.270	19.251	1.00	23.06
95	O	ILE	539	-0.047	56.183	19.773	1.00	24.41
96	CB	ILE	539	-1.882	54.630	21.329	1.00	22.83
97	CG1	ILE	539	-0.980	53.420	21.599	1.00	22.20
98	CG2	ILE	539	-3.272	54.416	21.956	1.00	28.20
99	CD1	ILE	539	-0.532	53.297	23.062	1.00	22.62
100	N	GLU	540	-0.226	54.598	18.192	1.00	26.89
101	CA	GLU	540	1.057	54.934	17.586	1.00	21.93
102	C	GLU	540	0.876	56.354	17.033	1.00	28.96
103	O	GLU	540	-0.099	56.649	16.351	1.00	29.21
104	CB	GLU	540	1.375	53.934	16.466	1.00	34.17
105	CG	GLU	540	2.763	54.039	15.856	1.00	34.86
106	CD	GLU	540	3.897	53.587	16.769	1.00	45.46
107	OE1	GLU	540	3.672	53.281	17.966	1.00	31.19
108	OE2	GLU	540	5.046	53.539	16.270	1.00	49.30
109	N	PRO	541	1.795	57.264	17.354	1.00	32.33
110	CA	PRO	541	1.659	58.635	16.856	1.00	34.70
111	C	PRO	541	1.667	58.767	15.331	1.00	30.39
112	O	PRO	541	2.212	57.925	14.636	1.00	27.63
113	CB	PRO	541	2.849	59.338	17.508	1.00	38.27
114	CG	PRO	541	3.883	58.205	17.590	1.00	40.07
115	CD	PRO	541	2.996	57.145	18.198	1.00	34.72
116	N	GLU	542	1.059	59.843	14.830	1.00	38.27
117	CA	GLU	542	1.016	60.116	13.393	1.00	35.46
118	C	GLU	542	2.448	60.549	13.036	1.00	35.96
119	O	GLU	542	3.146	61.098	13.878	1.00	30.43
120	CB	GLU	542	0.019	61.240	13.114	1.00	44.25
121	CG	GLU	542	0.362	62.659	13.675	1.00	99.90
122	CD	GLU	542	-0.666	63.779	13.498	1.00	99.90
123	OE1	GLU	542	-0.499	64.911	13.930	1.00	99.90
124	OE2	GLU	542	-1.781	63.396	12.815	1.00	99.90
125	N	VAL	543	2.894	60.309	11.807	1.00	32.80
126	CA	VAL	543	4.265	60.673	11.442	1.00	34.66
127	C	VAL	543	4.614	62.131	11.776	1.00	28.44
128	O	VAL	543	3.816	63.045	11.605	1.00	30.11
129	CB	VAL	543	4.552	60.403	9.937	1.00	41.68
130	CG1	VAL	543	3.962	61.509	9.080	1.00	38.06
131	CG2	VAL	543	6.058	60.258	9.715	1.00	45.80
132	N	LEU	544	5.823	62.324	12.280	1.00	30.17
133	CA	LEU	544	6.298	63.640	12.668	1.00	26.23
134	C	LEU	544	7.221	64.217	11.601	1.00	28.40
135	O	LEU	544	8.113	63.526	11.118	1.00	22.17

136	CB	LEU	544	7.089	63.668	14.010	1.00	28.58
137	CG	LEU	544	6.289	64.066	15.279	1.00	99.90
138	CD1	LEU	544	5.742	65.511	15.198	1.00	99.90
139	CD2	LEU	544	5.145	63.088	15.608	1.00	99.90
140	N	TYR	545	7.000	65.477	11.239	1.00	23.87
141	CA	TYR	545	7.839	66.165	10.260	1.00	27.94
142	C	TYR	545	8.960	66.895	10.979	1.00	28.04
143	O	TYR	545	8.794	67.338	12.116	1.00	24.24
144	CB	TYR	545	7.010	67.159	9.460	1.00	27.40
145	CG	TYR	545	6.083	66.476	8.487	1.00	34.60
146	CD1	TYR	545	4.825	66.038	8.889	1.00	37.81
147	CD2	TYR	545	6.489	66.207	7.181	1.00	38.29
148	CE1	TYR	545	3.992	65.348	8.016	1.00	47.26
149	CE2	TYR	545	5.661	65.516	6.295	1.00	39.38
150	CZ	TYR	545	4.414	65.090	6.724	1.00	41.71
151	OH	TYR	545	3.599	64.389	5.864	1.00	52.51
152	N	ALA	546	10.110	67.022	10.328	1.00	23.60
153	CA	ALA	546	11.213	67.720	10.964	1.00	26.37
154	C	ALA	546	11.100	69.231	10.756	1.00	29.47
155	O	ALA	546	11.688	70.011	11.510	1.00	28.14
156	CB	ALA	546	12.542	67.231	10.418	1.00	27.79
157	N	GLY	547	10.332	69.635	9.749	1.00	29.99
158	CA	GLY	547	10.213	71.051	9.439	1.00	32.21
159	C	GLY	547	11.541	71.501	8.836	1.00	39.13
160	O	GLY	547	11.964	72.645	8.992	1.00	40.76
161	N	TYR	548	12.206	70.581	8.140	1.00	38.38
162	CA	TYR	548	13.505	70.850	7.528	1.00	46.41
163	C	TYR	548	13.429	71.638	6.208	1.00	47.68
164	O	TYR	548	12.536	71.420	5.391	1.00	49.96
165	CB	TYR	548	14.242	69.521	7.333	1.00	42.73
166	CG	TYR	548	15.579	69.661	6.681	1.00	48.58
167	CD1	TYR	548	16.740	69.612	7.459	1.00	99.90
168	CD2	TYR	548	15.683	69.849	5.299	1.00	99.90
169	CE1	TYR	548	17.990	69.755	6.864	1.00	99.90
170	CE2	TYR	548	16.935	69.992	4.706	1.00	99.90
171	CZ	TYR	548	18.085	69.945	5.488	1.00	99.90
172	OH	TYR	548	19.311	70.089	4.902	1.00	99.90
173	N	ASP	549	14.389	72.543	6.016	1.00	51.90
174	CA	ASP	549	14.465	73.400	4.832	1.00	52.61
175	C	ASP	549	14.420	72.658	3.499	1.00	54.82
176	O	ASP	549	13.434	72.755	2.768	1.00	57.82
177	CB	ASP	549	15.727	74.257	4.903	1.00	52.84
178	CG	ASP	549	15.881	75.347	3.832	1.00	99.90
179	OD1	ASP	549	16.948	75.607	3.295	1.00	99.90
180	OD2	ASP	549	14.700	75.968	3.534	1.00	99.90
181	N	SER	550	15.499	71.940	3.190	1.00	55.70
182	CA	SER	550	15.638	71.176	1.951	1.00	56.60
183	C	SER	550	16.129	72.063	0.803	1.00	60.14

184	O	SER	550	17.143	71.764	0.160	1.00	61.18
185	CB	SER	550	14.308	70.509	1.579	1.00	57.02
186	OG	SER	550	13.309	71.449	1.168	1.00	99.90
187	N	SER	551	15.414	73.153	0.549	1.00	59.68
188	CA	SER	551	15.776	74.077	-0.525	1.00	60.50
189	C	SER	551	17.217	74.596	-0.418	1.00	61.78
190	O	SER	551	17.813	74.999	-1.421	1.00	61.98
191	CB	SER	551	14.797	75.251	-0.544	1.00	57.03
192	OG	SER	551	14.942	76.115	0.588	1.00	99.90
193	N	VAL	552	17.779	74.588	0.789	1.00	62.40
194	CA	VAL	552	19.146	75.067	0.984	1.00	64.42
195	C	VAL	552	20.127	73.906	1.141	1.00	66.61
196	O	VAL	552	19.730	72.783	1.477	1.00	64.83
197	CB	VAL	552	19.212	75.972	2.210	1.00	60.35
198	CG1	VAL	552	18.401	77.282	2.067	1.00	99.90
199	CG2	VAL	552	20.631	76.416	2.664	1.00	99.90
200	N	PRO	553	21.421	74.158	0.871	1.00	67.95
201	CA	PRO	553	22.478	73.146	0.982	1.00	69.09
202	C	PRO	553	22.696	72.762	2.450	1.00	68.98
203	O	PRO	553	23.139	73.581	3.258	1.00	70.54
204	CB	PRO	553	23.694	73.862	0.379	1.00	71.22
205	CG	PRO	553	23.056	74.901	-0.556	1.00	69.09
206	CD	PRO	553	22.000	75.422	0.389	1.00	68.58
207	N	ASP	554	22.391	71.512	2.783	1.00	68.95
208	CA	ASP	554	22.527	71.018	4.150	1.00	68.41
209	C	ASP	554	23.968	70.915	4.646	1.00	65.11
210	O	ASP	554	24.764	70.158	4.094	1.00	67.29
211	CB	ASP	554	21.883	69.631	4.276	1.00	72.12
212	CG	ASP	554	20.413	69.618	3.875	1.00	74.27
213	OD1	ASP	554	19.882	70.676	3.471	1.00	77.63
214	OD2	ASP	554	19.791	68.538	3.964	1.00	75.63
215	N	SER	555	24.301	71.673	5.689	1.00	61.36
216	CA	SER	555	25.640	71.597	6.262	1.00	54.04
217	C	SER	555	25.561	70.578	7.393	1.00	53.38
218	O	SER	555	24.471	70.198	7.818	1.00	44.49
219	CB	SER	555	26.118	72.959	6.830	1.00	56.37
220	OG	SER	555	25.403	73.353	8.005	1.00	99.90
221	N	THR	556	26.710	70.123	7.873	1.00	47.04
222	CA	THR	556	26.725	69.148	8.945	1.00	48.03
223	C	THR	556	26.006	69.688	10.180	1.00	44.05
224	O	THR	556	25.178	68.999	10.773	1.00	41.23
225	CB	THR	556	28.189	68.850	9.368	1.00	50.15
226	OG1	THR	556	28.903	68.203	8.319	1.00	99.90
227	CG2	THR	556	28.263	68.016	10.654	1.00	99.90
228	N	TRP	557	26.306	70.925	10.556	1.00	37.98
229	CA	TRP	557	25.673	71.524	11.726	1.00	39.84
230	C	TRP	557	24.187	71.832	11.510	1.00	37.46
231	O	TRP	557	23.393	71.743	12.449	1.00	35.48

232	CB	TRP	557	26.399	72.802	12.203	1.00	40.58
233	CG	TRP	557	26.434	73.958	11.232	1.00	99.90
234	CD1	TRP	557	27.544	74.313	10.390	1.00	99.90
235	CD2	TRP	557	25.452	74.961	11.022	1.00	99.90
236	NE1	TRP	557	27.245	75.473	9.684	1.00	99.90
237	CE2	TRP	557	25.973	75.857	10.063	1.00	99.90
238	CE3	TRP	557	24.158	75.198	11.599	1.00	99.90
239	CZ2	TRP	557	25.272	77.008	9.578	1.00	99.90
240	CZ3	TRP	557	23.408	76.344	11.133	1.00	99.90
241	CH2	TRP	557	23.957	77.238	10.130	1.00	99.90
242	N	ARG	558	23.800	72.201	10.291	1.00	36.47
243	CA	ARG	558	22.391	72.504	10.047	1.00	34.65
244	C	ARG	558	21.619	71.191	10.107	1.00	31.60
245	O	ARG	558	20.506	71.126	10.623	1.00	28.24
246	CB	ARG	558	22.184	73.186	8.679	1.00	35.58
247	CG	ARG	558	20.779	73.811	8.448	1.00	99.90
248	CD	ARG	558	20.649	74.442	7.052	1.00	99.90
249	NE	ARG	558	19.294	75.048	6.898	1.00	99.90
250	CZ	ARG	558	18.852	75.678	5.814	1.00	99.90
251	NH1	ARG	558	17.650	76.161	5.831	1.00	99.90
252	NH2	ARG	558	19.562	75.839	4.733	1.00	99.90
253	N	ILE	559	22.229	70.139	9.588	1.00	27.90
254	CA	ILE	559	21.613	68.820	9.602	1.00	29.29
255	C	ILE	559	21.345	68.364	11.043	1.00	28.57
256	O	ILE	559	20.232	67.953	11.369	1.00	25.88
257	CB	ILE	559	22.406	67.656	8.915	1.00	27.95
258	CG2	ILE	559	21.832	66.259	9.270	1.00	99.90
259	CG1	ILE	559	22.415	67.806	7.377	1.00	99.90
260	CD1	ILE	559	23.458	66.951	6.630	1.00	99.90
261	N	MET	560	22.364	68.445	11.894	1.00	25.56
262	CA	MET	560	22.212	68.046	13.295	1.00	24.24
263	C	MET	560	21.180	68.886	13.992	1.00	22.49
264	O	MET	560	20.386	68.365	14.764	1.00	21.35
265	CB	MET	560	23.550	68.151	14.056	1.00	24.95
266	CG	MET	560	24.525	67.005	13.723	1.00	99.90
267	SD	MET	560	23.920	65.411	14.376	1.00	99.90
268	CE	MET	560	24.920	64.276	13.373	1.00	99.90
269	N	THR	561	21.176	70.188	13.712	1.00	21.24
270	CA	THR	561	20.191	71.086	14.293	1.00	24.54
271	C	THR	561	18.791	70.654	13.870	1.00	24.54
272	O	THR	561	17.868	70.652	14.680	1.00	21.07
273	CB	THR	561	20.428	72.551	13.849	1.00	24.90
274	OG1	THR	561	21.608	73.099	14.433	1.00	26.56
275	CG2	THR	561	19.251	73.435	14.239	1.00	23.35
276	N	THR	562	18.623	70.304	12.598	1.00	19.11
277	CA	THR	562	17.325	69.852	12.125	1.00	21.51
278	C	THR	562	16.950	68.510	12.763	1.00	19.84
279	O	THR	562	15.765	68.271	13.043	1.00	21.66

280	CB	THR	562	17.209	69.868	10.626	1.00	24.02
281	OG1	THR	562	18.182	69.009	10.045	1.00	99.90
282	CG2	THR	562	17.280	71.338	10.099	1.00	99.90
283	N	LEU	563	17.928	67.625	12.974	1.00	18.47
284	CA	LEU	563	17.608	66.344	13.600	1.00	20.90
285	C	LEU	563	17.233	66.563	15.064	1.00	20.84
286	O	LEU	563	16.408	65.823	15.626	1.00	20.00
287	CB	LEU	563	18.779	65.376	13.501	1.00	17.55
288	CG	LEU	563	19.050	64.828	12.100	1.00	19.20
289	CD1	LEU	563	20.349	64.062	12.128	1.00	20.15
290	CD2	LEU	563	17.907	63.924	11.653	1.00	19.08
291	N	ASN	564	17.833	67.569	15.695	1.00	17.81
292	CA	ASN	564	17.467	67.856	17.098	1.00	19.99
293	C	ASN	564	16.053	68.424	17.186	1.00	18.99
294	O	ASN	564	15.333	68.155	18.142	1.00	20.08
295	CB	ASN	564	18.437	68.841	17.766	1.00	22.67
296	CG	ASN	564	19.770	68.211	18.120	1.00	27.38
297	OD1	ASN	564	19.868	66.996	18.368	1.00	24.69
298	ND2	ASN	564	20.855	69.103	18.180	1.00	23.33
299	N	MET	565	15.665	69.235	16.207	1.00	18.44
300	CA	MET	565	14.315	69.814	16.170	1.00	21.61
301	C	MET	565	13.323	68.659	16.001	1.00	23.93
302	O	MET	565	12.274	68.623	16.642	1.00	18.25
303	CB	MET	565	14.184	70.806	15.004	1.00	22.65
304	CG	MET	565	12.747	71.298	14.744	1.00	26.41
305	SD	MET	565	12.649	72.592	13.455	1.00	99.90
306	CE	MET	565	13.095	74.057	14.453	1.00	99.90
307	N	LEU	566	13.671	67.699	15.143	1.00	19.58
308	CA	LEU	566	12.817	66.527	14.951	1.00	17.13
309	C	LEU	566	12.746	65.757	16.277	1.00	16.29
310	O	LEU	566	11.671	65.324	16.696	1.00	19.55
311	CB	LEU	566	13.387	65.627	13.840	1.00	17.00
312	CG	LEU	566	12.612	64.333	13.581	1.00	19.10
313	CD1	LEU	566	11.169	64.658	13.155	1.00	18.65
314	CD2	LEU	566	13.358	63.527	12.488	1.00	17.08
315	N	GLY	567	13.893	65.600	16.928	1.00	16.83
316	CA	GLY	567	13.964	64.895	18.202	1.00	17.42
317	C	GLY	567	13.076	65.551	19.250	1.00	24.76
318	O	GLY	567	12.414	64.868	20.039	1.00	19.56
319	N	GLY	568	13.060	66.880	19.270	1.00	20.84
320	CA	GLY	568	12.208	67.618	20.227	1.00	22.88
321	C	GLY	568	10.745	67.300	19.943	1.00	23.92
322	O	GLY	568	9.941	67.105	20.861	1.00	23.22
323	N	ARG	569	10.383	67.247	18.663	1.00	17.75
324	CA	ARG	569	9.003	66.943	18.297	1.00	19.86
325	C	ARG	569	8.645	65.488	18.579	1.00	18.81
326	O	ARG	569	7.487	65.185	18.891	1.00	20.56
327	CB	ARG	569	8.759	67.252	16.822	1.00	18.63

328	CG	ARG	569	8.968	68.720	16.487	1.00	24.16
329	CD	ARG	569	8.809	68.967	15.007	1.00	28.88
330	NE	ARG	569	9.078	70.364	14.697	1.00	27.71
331	CZ	ARG	569	8.799	70.947	13.543	1.00	32.19
332	NH1	ARG	569	8.220	70.275	12.501	1.00	28.19
333	NH2	ARG	569	9.059	72.280	13.407	1.00	35.89
334	N	GLN	570	9.610	64.584	18.434	1.00	19.77
335	CA	GLN	570	9.347	63.185	18.733	1.00	19.30
336	C	GLN	570	9.290	62.930	20.235	1.00	21.49
337	O	GLN	570	8.579	62.041	20.686	1.00	21.43
338	CB	GLN	570	10.402	62.278	18.090	1.00	19.47
339	CG	GLN	570	10.243	62.249	16.570	1.00	22.41
340	CD	GLN	570	11.136	61.224	15.896	1.00	30.53
341	OE1	GLN	570	11.158	61.113	14.660	1.00	32.93
342	NE2	GLN	570	11.855	60.320	16.694	1.00	27.09
343	N	VAL	571	10.026	63.719	21.013	1.00	21.82
344	CA	VAL	571	10.012	63.557	22.464	1.00	22.79
345	C	VAL	571	8.605	63.860	22.974	1.00	21.40
346	O	VAL	571	8.070	63.124	23.814	1.00	23.41
347	CB	VAL	571	11.050	64.461	23.230	1.00	19.53
348	CG1	VAL	571	12.095	63.635	24.008	1.00	99.90
349	CG2	VAL	571	10.473	65.473	24.249	1.00	99.90
350	N	ILE	572	8.003	64.934	22.463	1.00	18.00
351	CA	ILE	572	6.645	65.281	22.849	1.00	19.91
352	C	ILE	572	5.737	64.105	22.494	1.00	24.23
353	O	ILE	572	4.905	63.659	23.291	1.00	19.07
354	CB	ILE	572	6.158	66.513	22.085	1.00	21.64
355	CG2	ILE	572	4.737	66.978	22.530	1.00	99.90
356	CG1	ILE	572	7.116	67.745	22.156	1.00	99.90
357	CD1	ILE	572	6.829	68.881	21.152	1.00	99.90
358	N	ALA	573	5.914	63.605	21.276	1.00	21.94
359	CA	ALA	573	5.113	62.497	20.783	1.00	21.38
360	C	ALA	573	5.250	61.280	21.696	1.00	20.10
361	O	ALA	573	4.249	60.628	22.014	1.00	22.32
362	CB	ALA	573	5.529	62.155	19.344	1.00	24.08
363	N	ALA	574	6.470	60.965	22.106	1.00	18.72
364	CA	ALA	574	6.727	59.847	23.015	1.00	20.27
365	C	ALA	574	6.016	59.998	24.355	1.00	18.31
366	O	ALA	574	5.435	59.040	24.866	1.00	19.16
367	CB	ALA	574	8.233	59.670	23.290	1.00	17.15
368	N	VAL	575	6.053	61.190	24.932	1.00	17.43
369	CA	VAL	575	5.395	61.372	26.212	1.00	21.44
370	C	VAL	575	3.881	61.250	26.044	1.00	19.86
371	O	VAL	575	3.229	60.652	26.888	1.00	21.47
372	CB	VAL	575	5.767	62.724	26.853	1.00	20.22
373	CG1	VAL	575	5.044	62.890	28.196	1.00	21.24
374	CG2	VAL	575	7.267	62.791	27.055	1.00	19.32
375	N	LYS	576	3.321	61.798	24.964	1.00	17.73

376	CA	LYS	576	1.887	61.669	24.724	1.00	22.58
377	C	LYS	576	1.511	60.201	24.534	1.00	23.23
378	O	LYS	576	0.505	59.724	25.073	1.00	20.64
379	CB	LYS	576	1.449	62.508	23.520	1.00	23.07
380	CG	LYS	576	1.382	64.007	23.862	1.00	25.92
381	CD	LYS	576	0.670	64.861	22.804	1.00	37.08
382	CE	LYS	576	1.481	65.021	21.529	1.00	48.50
383	NZ	LYS	576	0.886	65.984	20.514	1.00	49.18
384	N	TRP	577	2.324	59.485	23.767	1.00	18.73
385	CA	TRP	577	2.103	58.062	23.544	1.00	21.37
386	C	TRP	577	2.085	57.301	24.865	1.00	22.20
387	O	TRP	577	1.214	56.463	25.089	1.00	23.93
388	CB	TRP	577	3.212	57.516	22.647	1.00	21.47
389	CG	TRP	577	3.324	56.016	22.560	1.00	17.78
390	CD1	TRP	577	2.491	55.147	21.892	1.00	20.71
391	CD2	TRP	577	4.384	55.226	23.086	1.00	17.23
392	NE1	TRP	577	2.986	53.867	21.972	1.00	19.88
393	CE2	TRP	577	4.149	53.887	22.699	1.00	19.41
394	CE3	TRP	577	5.525	55.520	23.852	1.00	19.83
395	CZ2	TRP	577	5.018	52.839	23.050	1.00	18.15
396	CZ3	TRP	577	6.395	54.472	24.201	1.00	20.23
397	CH2	TRP	577	6.129	53.149	23.796	1.00	22.27
398	N	ALA	578	3.026	57.612	25.754	1.00	20.68
399	CA	ALA	578	3.119	56.904	27.029	1.00	22.57
400	C	ALA	578	1.893	57.109	27.916	1.00	20.83
401	O	ALA	578	1.580	56.253	28.722	1.00	22.59
402	CB	ALA	578	4.383	57.328	27.800	1.00	22.82
403	N	LYS	579	1.209	58.242	27.768	1.00	20.76
404	CA	LYS	579	0.034	58.523	28.591	1.00	25.82
405	C	LYS	579	-1.139	57.644	28.160	1.00	26.99
406	O	LYS	579	-2.099	57.463	28.917	1.00	24.98
407	CB	LYS	579	-0.343	60.011	28.504	1.00	27.35
408	CG	LYS	579	0.830	60.916	28.818	1.00	34.69
409	CD	LYS	579	0.432	62.175	29.587	1.00	44.84
410	CE	LYS	579	-0.567	63.030	28.838	1.00	49.64
411	NZ	LYS	579	-1.041	64.247	29.618	1.00	49.55
412	N	ALA	580	-1.063	57.101	26.947	1.00	23.17
413	CA	ALA	580	-2.110	56.201	26.454	1.00	23.40
414	C	ALA	580	-1.690	54.735	26.489	1.00	24.42
415	O	ALA	580	-2.505	53.841	26.216	1.00	21.97
416	CB	ALA	580	-2.504	56.563	25.016	1.00	24.11
417	N	ILE	581	-0.427	54.480	26.834	1.00	19.77
418	CA	ILE	581	0.106	53.112	26.852	1.00	21.02
419	C	ILE	581	-0.434	52.326	28.032	1.00	21.28
420	O	ILE	581	-0.175	52.679	29.172	1.00	22.53
421	CB	ILE	581	1.639	53.156	26.928	1.00	23.10
422	CG2	ILE	581	2.289	51.739	26.862	1.00	99.90
423	CG1	ILE	581	2.320	54.053	25.845	1.00	99.90

424	CD1	ILE	581	3.809	54.379	26.080	1.00	99.90
425	N	PRO	582	-1.142	51.218	27.773	1.00	22.85
426	CA	PRO	582	-1.688	50.455	28.903	1.00	24.25
427	C	PRO	582	-0.693	50.121	30.008	1.00	25.32
428	O	PRO	582	0.380	49.563	29.756	1.00	25.05
429	CB	PRO	582	-2.273	49.215	28.221	1.00	24.36
430	CG	PRO	582	-2.742	49.779	26.893	1.00	23.83
431	CD	PRO	582	-1.474	50.547	26.502	1.00	20.46
432	N	GLY	583	-1.064	50.493	31.233	1.00	25.15
433	CA	GLY	583	-0.240	50.226	32.397	1.00	25.65
434	C	GLY	583	0.794	51.272	32.770	1.00	23.09
435	O	GLY	583	1.172	51.397	33.932	1.00	25.86
436	N	PHE	584	1.247	52.055	31.804	1.00	22.74
437	CA	PHE	584	2.289	53.021	32.116	1.00	23.63
438	C	PHE	584	1.874	54.103	33.106	1.00	22.42
439	O	PHE	584	2.605	54.395	34.041	1.00	21.78
440	CB	PHE	584	2.800	53.696	30.832	1.00	21.38
441	CG	PHE	584	4.125	54.391	31.005	1.00	20.80
442	CD1	PHE	584	5.284	53.639	31.225	1.00	22.81
443	CD2	PHE	584	4.221	55.780	30.956	1.00	24.10
444	CE1	PHE	584	6.512	54.254	31.389	1.00	24.39
445	CE2	PHE	584	5.458	56.409	31.121	1.00	19.38
446	CZ	PHE	584	6.597	55.644	31.336	1.00	23.48
447	N	ARG	585	0.696	54.688	32.899	1.00	22.15
448	CA	ARG	585	0.230	55.780	33.752	1.00	25.70
449	C	ARG	585	0.022	55.358	35.192	1.00	24.37
450	O	ARG	585	-0.142	56.197	36.080	1.00	24.34
451	CB	ARG	585	-1.081	56.353	33.225	1.00	23.04
452	CG	ARG	585	-2.193	55.320	33.145	1.00	24.68
453	CD	ARG	585	-3.541	56.001	32.956	1.00	25.40
454	NE	ARG	585	-4.603	55.003	32.931	1.00	24.48
455	CZ	ARG	585	-5.894	55.292	32.940	1.00	20.47
456	NH1	ARG	585	-6.370	56.573	33.000	1.00	23.59
457	NH2	ARG	585	-6.788	54.265	32.887	1.00	26.38
458	N	ASN	586	0.040	54.056	35.420	1.00	27.20
459	CA	ASN	586	-0.174	53.518	36.748	1.00	23.55
460	C	ASN	586	1.103	53.371	37.564	1.00	26.53
461	O	ASN	586	1.037	53.106	38.766	1.00	27.16
462	CB	ASN	586	-0.930	52.210	36.617	1.00	32.06
463	CG	ASN	586	-2.263	52.399	35.915	1.00	33.85
464	OD1	ASN	586	-2.792	51.484	35.293	1.00	37.94
465	ND2	ASN	586	-3.004	53.573	36.197	1.00	28.27
466	N	LEU	587	2.256	53.542	36.920	1.00	22.63
467	CA	LEU	587	3.532	53.511	37.620	1.00	22.51
468	C	LEU	587	3.617	54.863	38.294	1.00	19.73
469	O	LEU	587	2.941	55.801	37.907	1.00	23.16
470	CB	LEU	587	4.713	53.393	36.649	1.00	21.95
471	CG	LEU	587	4.686	52.151	35.762	1.00	20.73

472	CD1	LEU	587	5.770	52.276	34.661	1.00	23.47
473	CD2	LEU	587	4.890	50.905	36.624	1.00	22.85
474	N	HIS	588	4.454	54.948	39.308	1.00	21.02
475	CA	HIS	588	4.661	56.192	40.037	1.00	25.86
476	C	HIS	588	5.125	57.217	39.005	1.00	26.17
477	O	HIS	588	5.834	56.860	38.072	1.00	23.09
478	CB	HIS	588	5.727	55.921	41.100	1.00	28.77
479	CG	HIS	588	5.930	57.038	42.066	1.00	36.70
480	ND1	HIS	588	6.543	58.220	41.718	1.00	34.14
481	CD2	HIS	588	5.612	57.149	43.377	1.00	38.95
482	CE1	HIS	588	6.598	59.012	42.775	1.00	39.45
483	NE2	HIS	588	6.039	58.385	43.794	1.00	39.37
484	N	LEU	589	4.717	58.477	39.156	1.00	20.73
485	CA	LEU	589	5.113	59.520	38.215	1.00	27.73
486	C	LEU	589	6.627	59.635	38.061	1.00	27.07
487	O	LEU	589	7.137	59.841	36.948	1.00	24.14
488	CB	LEU	589	4.534	60.892	38.625	1.00	26.09
489	CG	LEU	589	2.993	61.022	38.767	1.00	99.90
490	CD1	LEU	589	2.612	62.479	39.068	1.00	99.90
491	CD2	LEU	589	2.238	60.537	37.518	1.00	99.90
492	N	ASP	590	7.362	59.511	39.164	1.00	24.97
493	CA	ASP	590	8.811	59.597	39.074	1.00	27.70
494	C	ASP	590	9.369	58.468	38.212	1.00	25.79
495	O	ASP	590	10.365	58.653	37.515	1.00	26.38
496	CB	ASP	590	9.479	59.536	40.452	1.00	33.81
497	CG	ASP	590	9.143	60.731	41.321	1.00	46.44
498	OD1	ASP	590	8.821	61.801	40.763	1.00	51.31
499	OD2	ASP	590	9.238	60.609	42.566	1.00	50.96
500	N	ASP	591	8.744	57.299	38.279	1.00	23.70
501	CA	ASP	591	9.199	56.177	37.478	1.00	22.43
502	C	ASP	591	8.872	56.433	36.012	1.00	19.90
503	O	ASP	591	9.691	56.138	35.140	1.00	22.60
504	CB	ASP	591	8.551	54.870	37.911	1.00	21.92
505	CG	ASP	591	8.827	54.538	39.355	1.00	33.42
506	OD1	ASP	591	9.882	54.978	39.884	1.00	34.56
507	OD2	ASP	591	7.996	53.817	39.949	1.00	39.54
508	N	GLN	592	7.698	57.001	35.742	1.00	19.31
509	CA	GLN	592	7.307	57.263	34.357	1.00	17.71
510	C	GLN	592	8.321	58.215	33.762	1.00	23.99
511	O	GLN	592	8.813	57.992	32.663	1.00	19.91
512	CB	GLN	592	5.924	57.901	34.270	1.00	19.37
513	CG	GLN	592	4.823	57.083	34.901	1.00	22.18
514	CD	GLN	592	3.473	57.742	34.779	1.00	22.76
515	OE1	GLN	592	2.619	57.600	35.656	1.00	25.01
516	NE2	GLN	592	3.183	58.456	33.594	1.00	18.79
517	N	MET	593	8.623	59.289	34.485	1.00	21.08
518	CA	MET	593	9.602	60.249	33.999	1.00	21.96
519	C	MET	593	10.973	59.607	33.797	1.00	24.64

520	O	MET	593	11.599	59.811	32.755	1.00	23.28
521	CB	MET	593	9.727	61.448	34.968	1.00	25.55
522	CG	MET	593	8.454	62.300	35.153	1.00	99.90
523	SD	MET	593	8.851	63.799	36.068	1.00	99.90
524	CE	MET	593	7.176	64.333	36.445	1.00	99.90
525	N	THR	594	11.439	58.840	34.785	1.00	19.75
526	CA	THR	594	12.733	58.166	34.705	1.00	20.18
527	C	THR	594	12.812	57.212	33.499	1.00	19.01
528	O	THR	594	13.815	57.184	32.799	1.00	18.23
529	CB	THR	594	13.014	57.344	35.986	1.00	24.15
530	OG1	THR	594	13.099	58.173	37.142	1.00	26.23
531	CG2	THR	594	14.347	56.633	35.879	1.00	23.53
532	N	LEU	595	11.761	56.428	33.256	1.00	17.46
533	CA	LEU	595	11.778	55.502	32.116	1.00	19.07
534	C	LEU	595	11.867	56.218	30.760	1.00	17.18
535	O	LEU	595	12.533	55.729	29.840	1.00	17.28
536	CB	LEU	595	10.544	54.590	32.139	1.00	18.92
537	CG	LEU	595	10.566	53.657	33.371	1.00	22.74
538	CD1	LEU	595	9.226	52.941	33.555	1.00	22.99
539	CD2	LEU	595	11.672	52.663	33.188	1.00	20.48
540	N	LEU	596	11.172	57.343	30.631	1.00	16.29
541	CA	LEU	596	11.231	58.127	29.386	1.00	23.76
542	C	LEU	596	12.630	58.735	29.234	1.00	22.00
543	O	LEU	596	13.213	58.713	28.148	1.00	17.05
544	CB	LEU	596	10.153	59.246	29.361	1.00	18.60
545	CG	LEU	596	8.665	58.830	29.513	1.00	99.90
546	CD1	LEU	596	7.756	60.057	29.351	1.00	99.90
547	CD2	LEU	596	8.247	57.740	28.512	1.00	99.90
548	N	GLN	597	13.180	59.275	30.318	1.00	21.43
549	CA	GLN	597	14.516	59.863	30.216	1.00	23.26
550	C	GLN	597	15.596	58.825	29.922	1.00	22.82
551	O	GLN	597	16.616	59.155	29.340	1.00	22.26
552	CB	GLN	597	14.856	60.678	31.478	1.00	21.04
553	CG	GLN	597	13.846	61.816	31.674	1.00	26.41
554	CD	GLN	597	14.176	62.744	32.833	1.00	34.88
555	OE1	GLN	597	14.610	62.307	33.897	1.00	28.80
556	NE2	GLN	597	13.918	64.117	32.626	1.00	32.80
557	N	TYR	598	15.376	57.571	30.312	1.00	21.10
558	CA	TYR	598	16.362	56.521	30.034	1.00	23.73
559	C	TYR	598	16.240	55.998	28.622	1.00	21.41
560	O	TYR	598	17.233	55.689	27.968	1.00	24.76
561	CB	TYR	598	16.150	55.309	30.946	1.00	22.41
562	CG	TYR	598	16.647	55.443	32.367	1.00	21.14
563	CD1	TYR	598	17.195	56.628	32.840	1.00	22.56
564	CD2	TYR	598	16.589	54.356	33.230	1.00	25.54
565	CE1	TYR	598	17.682	56.729	34.154	1.00	27.58
566	CE2	TYR	598	17.068	54.442	34.533	1.00	23.54
567	CZ	TYR	598	17.612	55.626	34.989	1.00	22.36

568	OH	TYR	598	18.085	55.737	36.276	1.00	29.42
569	N	SER	599	15.014	55.934	28.138	1.00	19.69
570	CA	SER	599	14.784	55.299	26.849	1.00	21.05
571	C	SER	599	14.475	56.110	25.608	1.00	20.67
572	O	SER	599	14.363	55.519	24.520	1.00	17.40
573	CB	SER	599	13.657	54.283	27.020	1.00	24.21
574	OG	SER	599	12.387	54.913	27.142	1.00	27.35
575	N	TRP	600	14.371	57.430	25.724	1.00	17.55
576	CA	TRP	600	13.998	58.207	24.546	1.00	21.93
577	C	TRP	600	14.874	57.931	23.320	1.00	18.91
578	O	TRP	600	14.350	57.773	22.223	1.00	20.07
579	CB	TRP	600	13.972	59.717	24.836	1.00	22.52
580	CG	TRP	600	15.298	60.318	25.168	1.00	23.08
581	CD1	TRP	600	15.904	60.348	26.389	1.00	28.21
582	CD2	TRP	600	16.200	60.938	24.252	1.00	24.51
583	NE1	TRP	600	17.137	60.953	26.292	1.00	25.19
584	CE2	TRP	600	17.342	61.325	24.989	1.00	26.64
585	CE3	TRP	600	16.154	61.203	22.880	1.00	25.75
586	CZ2	TRP	600	18.442	61.969	24.396	1.00	29.86
587	CZ3	TRP	600	17.249	61.843	22.288	1.00	32.59
588	CH2	TRP	600	18.375	62.218	23.048	1.00	30.85
589	N	MET	601	16.191	57.861	23.495	1.00	21.38
590	CA	MET	601	17.087	57.622	22.352	1.00	18.69
591	C	MET	601	16.823	56.265	21.715	1.00	23.20
592	O	MET	601	16.790	56.138	20.478	1.00	21.19
593	CB	MET	601	18.553	57.684	22.783	1.00	21.49
594	CG	MET	601	19.522	57.518	21.611	1.00	22.22
595	SD	MET	601	19.630	59.001	20.532	1.00	27.03
596	CE	MET	601	20.664	60.086	21.623	1.00	26.64
597	N	PHE	602	16.668	55.248	22.557	1.00	19.23
598	CA	PHE	602	16.383	53.904	22.078	1.00	22.32
599	C	PHE	602	15.085	53.867	21.295	1.00	20.68
600	O	PHE	602	15.028	53.277	20.224	1.00	21.09
601	CB	PHE	602	16.113	52.858	23.210	1.00	23.54
602	CG	PHE	602	17.192	52.587	24.232	1.00	99.90
603	CD1	PHE	602	17.625	53.578	25.189	1.00	99.90
604	CD2	PHE	602	17.732	51.253	24.325	1.00	99.90
605	CE1	PHE	602	18.605	53.248	26.189	1.00	99.90
606	CE2	PHE	602	18.716	50.929	25.313	1.00	99.90
607	CZ	PHE	602	19.158	51.927	26.246	1.00	99.90
608	N	LEU	603	14.035	54.487	21.830	1.00	20.06
609	CA	LEU	603	12.735	54.478	21.165	1.00	16.39
610	C	LEU	603	12.804	55.201	19.831	1.00	18.68
611	O	LEU	603	12.226	54.754	18.838	1.00	18.94
612	CB	LEU	603	11.679	55.173	22.038	1.00	14.15
613	CG	LEU	603	11.408	54.532	23.397	1.00	20.53
614	CD1	LEU	603	10.488	55.448	24.208	1.00	20.07
615	CD2	LEU	603	10.742	53.165	23.186	1.00	24.11

616	N	MET	604	13.503	56.329	19.810	1.00	18.42
617	CA	MET	604	13.597	57.094	18.587	1.00	19.21
618	C	MET	604	14.437	56.424	17.504	1.00	19.93
619	O	MET	604	14.071	56.492	16.322	1.00	23.09
620	CB	MET	604	14.113	58.499	18.889	1.00	21.20
621	CG	MET	604	13.084	59.331	19.684	1.00	21.45
622	SD	MET	604	13.619	61.014	19.956	1.00	25.97
623	CE	MET	604	12.389	61.557	21.170	1.00	26.52
624	N	ALA	605	15.545	55.793	17.873	1.00	18.66
625	CA	ALA	605	16.357	55.125	16.843	1.00	19.71
626	C	ALA	605	15.628	53.865	16.343	1.00	22.38
627	O	ALA	605	15.752	53.486	15.178	1.00	18.63
628	CB	ALA	605	17.774	54.744	17.363	1.00	20.60
629	N	PHE	606	14.871	53.230	17.233	1.00	18.16
630	CA	PHE	606	14.092	52.032	16.886	1.00	20.65
631	C	PHE	606	13.005	52.461	15.884	1.00	21.25
632	O	PHE	606	12.762	51.773	14.879	1.00	23.39
633	CB	PHE	606	13.479	51.439	18.173	1.00	19.84
634	CG	PHE	606	13.048	49.979	18.055	1.00	22.22
635	CD1	PHE	606	13.982	48.980	17.790	1.00	22.72
636	CD2	PHE	606	11.719	49.613	18.255	1.00	23.08
637	CE1	PHE	606	13.609	47.639	17.726	1.00	23.74
638	CE2	PHE	606	11.325	48.274	18.196	1.00	24.95
639	CZ	PHE	606	12.266	47.287	17.930	1.00	22.67
640	N	ALA	607	12.352	53.591	16.160	1.00	18.00
641	CA	ALA	607	11.335	54.114	15.266	1.00	19.15
642	C	ALA	607	11.932	54.472	13.914	1.00	19.60
643	O	ALA	607	11.307	54.266	12.866	1.00	17.94
644	CB	ALA	607	10.674	55.315	15.963	1.00	99.90
645	N	LEU	608	13.135	55.044	13.939	1.00	18.18
646	CA	LEU	608	13.841	55.382	12.710	1.00	18.82
647	C	LEU	608	14.041	54.100	11.907	1.00	20.32
648	O	LEU	608	13.869	54.087	10.671	1.00	21.06
649	CB	LEU	608	15.201	55.995	13.046	1.00	18.85
650	CG	LEU	608	16.256	56.031	11.928	1.00	15.12
651	CD1	LEU	608	15.824	56.992	10.845	1.00	21.31
652	CD2	LEU	608	17.592	56.443	12.524	1.00	22.01
653	N	GLY	609	14.406	53.031	12.610	1.00	19.32
654	CA	GLY	609	14.642	51.749	11.967	1.00	22.15
655	C	GLY	609	13.388	51.267	11.274	1.00	22.09
656	O	GLY	609	13.404	50.859	10.095	1.00	18.52
657	N	TRP	610	12.274	51.326	11.995	1.00	18.65
658	CA	TRP	610	11.011	50.885	11.424	1.00	21.70
659	C	TRP	610	10.602	51.712	10.189	1.00	20.69
660	O	TRP	610	10.218	51.156	9.162	1.00	20.73
661	CB	TRP	610	9.911	50.926	12.493	1.00	19.80
662	CG	TRP	610	8.584	50.462	11.980	1.00	20.60
663	CD1	TRP	610	7.541	51.236	11.588	1.00	26.35

664	CD2	TRP	610	8.204	49.104	11.712	1.00	22.75
665	NE1	TRP	610	6.527	50.452	11.086	1.00	25.80
666	CE2	TRP	610	6.909	49.137	11.151	1.00	27.72
667	CE3	TRP	610	8.835	47.870	11.890	1.00	24.76
668	CZ2	TRP	610	6.223	47.971	10.759	1.00	28.33
669	CZ3	TRP	610	8.154	46.703	11.502	1.00	25.79
670	CH2	TRP	610	6.862	46.771	10.944	1.00	23.99
671	N	ARG	611	10.686	53.038	10.273	1.00	20.81
672	CA	ARG	611	10.301	53.868	9.132	1.00	18.86
673	C	ARG	611	11.209	53.618	7.926	1.00	18.44
674	O	ARG	611	10.747	53.594	6.783	1.00	20.30
675	CB	ARG	611	10.341	55.357	9.493	1.00	18.28
676	CG	ARG	611	9.298	55.794	10.543	1.00	20.05
677	CD	ARG	611	9.320	57.317	10.695	1.00	25.08
678	NE	ARG	611	10.593	57.831	11.202	1.00	20.13
679	CZ	ARG	611	10.944	57.862	12.483	1.00	22.33
680	NH1	ARG	611	10.128	57.409	13.478	1.00	22.73
681	NH2	ARG	611	12.160	58.356	12.800	1.00	19.31
682	N	SER	612	12.490	53.431	8.187	1.00	20.91
683	CA	SER	612	13.459	53.185	7.117	1.00	18.59
684	C	SER	612	13.126	51.856	6.432	1.00	24.76
685	O	SER	612	13.088	51.761	5.208	1.00	19.96
686	CB	SER	612	14.869	53.159	7.709	1.00	19.66
687	OG	SER	612	15.287	54.391	8.280	1.00	23.01
688	N	TYR	613	12.852	50.847	7.248	1.00	20.64
689	CA	TYR	613	12.468	49.520	6.762	1.00	21.51
690	C	TYR	613	11.193	49.603	5.909	1.00	20.49
691	O	TYR	613	11.166	49.176	4.749	1.00	20.85
692	CB	TYR	613	12.255	48.625	7.993	1.00	20.88
693	CG	TYR	613	11.481	47.341	7.799	1.00	24.41
694	CD1	TYR	613	11.853	46.392	6.843	1.00	24.71
695	CD2	TYR	613	10.448	47.022	8.672	1.00	22.00
696	CE1	TYR	613	11.208	45.137	6.787	1.00	21.58
697	CE2	TYR	613	9.812	45.792	8.622	1.00	21.74
698	CZ	TYR	613	10.203	44.853	7.691	1.00	24.16
699	OH	TYR	613	9.579	43.627	7.637	1.00	22.86
700	N	ARG	614	10.147	50.203	6.467	1.00	19.61
701	CA	ARG	614	8.859	50.302	5.779	1.00	20.88
702	C	ARG	614	8.783	51.149	4.525	1.00	25.83
703	O	ARG	614	8.173	50.737	3.535	1.00	23.20
704	CB	ARG	614	7.789	50.821	6.744	1.00	26.26
705	CG	ARG	614	7.402	49.864	7.838	1.00	29.74
706	CD	ARG	614	6.455	48.756	7.353	1.00	34.33
707	NE	ARG	614	6.095	47.866	8.496	1.00	99.90
708	CZ	ARG	614	5.290	46.810	8.424	1.00	99.90
709	NH1	ARG	614	5.065	46.135	9.507	1.00	99.90
710	NH2	ARG	614	4.714	46.415	7.324	1.00	99.90
711	N	GLN	615	9.397	52.326	4.564	1.00	20.34

712	CA	GLN	615	9.314	53.278	3.458	1.00	25.32
713	C	GLN	615	10.398	53.227	2.392	1.00	24.30
714	O	GLN	615	10.153	53.590	1.243	1.00	23.64
715	CB	GLN	615	9.274	54.708	4.027	1.00	25.43
716	CG	GLN	615	9.138	55.864	2.982	1.00	99.90
717	CD	GLN	615	9.152	57.318	3.470	1.00	99.90
718	OE1	GLN	615	9.089	58.249	2.682	1.00	99.90
719	NE2	GLN	615	9.259	57.578	4.749	1.00	99.90
720	N	SER	616	11.596	52.791	2.759	1.00	24.39
721	CA	SER	616	12.680	52.765	1.789	1.00	25.76
722	C	SER	616	13.443	51.452	1.809	1.00	24.92
723	O	SER	616	14.609	51.399	1.451	1.00	27.56
724	CB	SER	616	13.650	53.978	2.014	1.00	27.85
725	OG	SER	616	14.409	53.867	3.223	1.00	99.90
726	N	SER	617	12.763	50.384	2.217	1.00	22.68
727	CA	SER	617	13.365	49.052	2.280	1.00	24.24
728	C	SER	617	14.686	48.997	3.021	1.00	22.19
729	O	SER	617	15.547	48.160	2.721	1.00	24.35
730	CB	SER	617	13.526	48.483	0.862	1.00	22.79
731	OG	SER	617	12.294	48.353	0.151	1.00	24.02
732	N	ALA	618	14.827	49.883	4.011	1.00	20.76
733	CA	ALA	618	16.026	49.916	4.830	1.00	21.80
734	C	ALA	618	17.254	50.449	4.123	1.00	20.80
735	O	ALA	618	18.352	50.403	4.676	1.00	25.34
736	CB	ALA	618	16.235	48.506	5.409	1.00	99.90
737	N	ASN	619	17.069	50.990	2.928	1.00	23.07
738	CA	ASN	619	18.203	51.479	2.156	1.00	23.42
739	C	ASN	619	18.560	52.962	2.319	1.00	25.60
740	O	ASN	619	19.512	53.440	1.703	1.00	23.56
741	CB	ASN	619	17.987	51.138	0.680	1.00	25.32
742	CG	ASN	619	17.774	49.661	0.332	1.00	99.90
743	OD1	ASN	619	16.665	49.194	0.123	1.00	99.90
744	ND2	ASN	619	18.813	48.871	0.281	1.00	99.90
745	N	LEU	620	17.787	53.687	3.121	1.00	21.96
746	CA	LEU	620	18.074	55.094	3.425	1.00	22.20
747	C	LEU	620	17.560	55.257	4.857	1.00	24.08
748	O	LEU	620	16.807	54.408	5.327	1.00	21.84
749	CB	LEU	620	17.311	56.048	2.499	1.00	23.95
750	CG	LEU	620	17.531	55.912	0.968	1.00	99.90
751	CD1	LEU	620	16.772	57.020	0.225	1.00	99.90
752	CD2	LEU	620	19.018	55.951	0.576	1.00	99.90
753	N	LEU	621	17.985	56.311	5.552	1.00	21.78
754	CA	LEU	621	17.505	56.553	6.924	1.00	22.28
755	C	LEU	621	16.356	57.545	6.837	1.00	20.07
756	O	LEU	621	16.541	58.727	6.544	1.00	21.05
757	CB	LEU	621	18.630	57.076	7.826	1.00	21.10
758	CG	LEU	621	19.759	56.060	8.074	1.00	24.71
759	CD1	LEU	621	20.794	56.627	9.017	1.00	26.09

760	CD2	LEU	621	19.174	54.777	8.653	1.00	23.43
761	N	CYS	622	15.154	57.041	7.070	1.00	20.52
762	CA	CYS	622	13.950	57.844	6.975	1.00	17.48
763	C	CYS	622	13.647	58.516	8.327	1.00	21.46
764	O	CYS	622	12.783	58.069	9.066	1.00	18.14
765	CB	CYS	622	12.729	57.025	6.493	1.00	20.38
766	SG	CYS	622	12.923	56.304	4.826	1.00	99.90
767	N	PHE	623	14.377	59.583	8.644	1.00	20.19
768	CA	PHE	623	14.147	60.288	9.903	1.00	22.33
769	C	PHE	623	12.734	60.881	9.946	1.00	19.77
770	O	PHE	623	12.036	60.799	10.953	1.00	20.69
771	CB	PHE	623	15.209	61.386	10.109	1.00	17.81
772	CG	PHE	623	16.565	60.855	10.420	1.00	19.78
773	CD1	PHE	623	17.463	60.544	9.409	1.00	26.89
774	CD2	PHE	623	16.942	60.616	11.737	1.00	21.49
775	CE1	PHE	623	18.726	59.999	9.722	1.00	24.89
776	CE2	PHE	623	18.193	60.073	12.051	1.00	21.92
777	CZ	PHE	623	19.087	59.766	11.043	1.00	25.29
778	N	ALA	624	12.311	61.478	8.846	1.00	18.84
779	CA	ALA	624	10.976	62.054	8.755	1.00	18.94
780	C	ALA	624	10.706	62.148	7.259	1.00	23.24
781	O	ALA	624	11.621	61.956	6.458	1.00	21.88
782	CB	ALA	624	10.948	63.442	9.399	1.00	19.00
783	N	PRO	625	9.452	62.382	6.864	1.00	24.08
784	CA	PRO	625	9.122	62.493	5.441	1.00	22.75
785	C	PRO	625	9.897	63.631	4.757	1.00	31.17
786	O	PRO	625	10.189	63.558	3.560	1.00	27.19
787	CB	PRO	625	7.618	62.742	5.476	1.00	23.42
788	CG	PRO	625	7.198	61.973	6.719	1.00	29.68
789	CD	PRO	625	8.225	62.532	7.668	1.00	19.66
790	N	ASP	626	10.240	64.671	5.514	1.00	24.25
791	CA	ASP	626	10.984	65.801	4.951	1.00	30.35
792	C	ASP	626	12.470	65.758	5.305	1.00	28.45
793	O	ASP	626	13.216	66.724	5.082	1.00	31.54
794	CB	ASP	626	10.362	67.106	5.439	1.00	33.03
795	CG	ASP	626	10.455	67.270	6.945	1.00	42.61
796	OD1	ASP	626	10.274	66.273	7.681	1.00	37.30
797	OD2	ASP	626	10.687	68.409	7.395	1.00	39.66
798	N	LEU	627	12.907	64.627	5.844	1.00	25.42
799	CA	LEU	627	14.290	64.464	6.238	1.00	23.61
800	C	LEU	627	14.689	62.992	6.078	1.00	25.27
801	O	LEU	627	14.650	62.200	7.018	1.00	21.60
802	CB	LEU	627	14.465	64.921	7.686	1.00	25.81
803	CG	LEU	627	15.903	65.214	8.098	1.00	26.41
804	CD1	LEU	627	16.471	66.222	7.110	1.00	37.20
805	CD2	LEU	627	15.944	65.796	9.499	1.00	23.25
806	N	ILE	628	15.038	62.634	4.849	1.00	20.00
807	CA	ILE	628	15.447	61.288	4.510	1.00	21.82

808	C	ILE	628	16.926	61.365	4.132	1.00	26.37
809	O	ILE	628	17.280	62.120	3.233	1.00	27.10
810	CB	ILE	628	14.659	60.791	3.287	1.00	19.86
811	CG1	ILE	628	13.160	60.854	3.576	1.00	23.93
812	CG2	ILE	628	15.107	59.369	2.935	1.00	26.69
813	CD1	ILE	628	12.264	60.752	2.345	1.00	22.62
814	N	ILE	629	17.781	60.593	4.797	1.00	24.00
815	CA	ILE	629	19.203	60.626	4.478	1.00	30.39
816	C	ILE	629	19.745	59.395	3.756	1.00	28.22
817	O	ILE	629	19.446	58.251	4.116	1.00	27.38
818	CB	ILE	629	19.971	60.933	5.814	1.00	27.74
819	CG2	ILE	629	21.443	61.321	5.592	1.00	99.90
820	CG1	ILE	629	19.354	62.070	6.698	1.00	99.90
821	CD1	ILE	629	19.296	63.491	6.094	1.00	99.90
822	N	ASN	630	20.560	59.665	2.739	1.00	37.87
823	CA	ASN	630	21.239	58.635	1.955	1.00	34.28
824	C	ASN	630	22.728	58.921	2.135	1.00	40.43
825	O	ASN	630	23.105	59.961	2.699	1.00	32.88
826	CB	ASN	630	20.868	58.724	0.473	1.00	43.78
827	CG	ASN	630	21.147	60.091	-0.113	1.00	39.05
828	OD1	ASN	630	22.203	60.674	0.123	1.00	56.25
829	ND2	ASN	630	20.136	60.626	-0.936	1.00	55.74
830	N	GLU	631	23.563	58.000	1.660	1.00	37.34
831	CA	GLU	631	25.015	58.123	1.773	1.00	41.84
832	C	GLU	631	25.558	59.475	1.335	1.00	36.02
833	O	GLU	631	26.437	60.024	1.991	1.00	37.52
834	CB	GLU	631	25.716	57.026	0.967	1.00	43.26
835	CG	GLU	631	25.473	55.592	1.439	1.00	53.06
836	CD	GLU	631	24.088	55.065	1.099	1.00	52.18
837	OE1	GLU	631	23.252	55.830	0.573	1.00	55.65
838	OE2	GLU	631	23.838	53.869	1.359	1.00	59.59
839	N	GLN	632	25.040	60.004	0.229	1.00	37.37
840	CA	GLN	632	25.483	61.297	-0.301	1.00	41.31
841	C	GLN	632	25.334	62.468	0.673	1.00	44.67
842	O	GLN	632	26.122	63.416	0.642	1.00	39.36
843	CB	GLN	632	24.710	61.641	-1.575	1.00	39.63
844	CG	GLN	632	24.887	60.656	-2.720	1.00	54.67
845	CD	GLN	632	23.944	60.939	-3.875	1.00	54.04
846	OE1	GLN	632	24.051	61.964	-4.552	1.00	65.04
847	NE2	GLN	632	22.945	59.973	-4.120	1.00	58.37
848	N	ARG	633	24.327	62.401	1.538	1.00	42.38
849	CA	ARG	633	24.072	63.483	2.483	1.00	46.01
850	C	ARG	633	24.797	63.327	3.817	1.00	44.06
851	O	ARG	633	24.707	64.194	4.690	1.00	43.28
852	CB	ARG	633	22.560	63.614	2.701	1.00	45.62
853	CG	ARG	633	21.804	63.732	1.385	1.00	51.99
854	CD	ARG	633	20.303	63.885	1.551	1.00	54.00
855	NE	ARG	633	19.923	65.164	2.148	1.00	62.20

856	CZ	ARG	633	18.664	65.565	2.312	1.00	62.82
857	NH1	ARG	633	17.623	64.842	1.808	1.00	63.08
858	NH2	ARG	633	18.318	66.680	2.975	1.00	64.33
859	N	MET	634	25.524	62.231	3.972	1.00	42.60
860	CA	MET	634	26.267	61.991	5.200	1.00	44.82
861	C	MET	634	27.734	62.253	4.897	1.00	44.81
862	O	MET	634	28.533	61.322	4.802	1.00	41.79
863	CB	MET	634	26.074	60.546	5.653	1.00	47.11
864	CG	MET	634	24.619	60.166	5.850	1.00	38.54
865	SD	MET	634	24.425	58.402	6.144	1.00	40.15
866	CE	MET	634	22.638	58.288	6.218	1.00	40.02
867	N	THR	635	28.077	63.525	4.733	1.00	45.90
868	CA	THR	635	29.448	63.911	4.417	1.00	49.64
869	C	THR	635	30.366	63.686	5.604	1.00	52.38
870	O	THR	635	31.373	62.981	5.505	1.00	56.13
871	CB	THR	635	29.493	65.382	4.014	1.00	52.46
872	OG1	THR	635	28.707	65.604	2.851	1.00	99.90
873	CG2	THR	635	30.883	65.951	3.656	1.00	99.90
874	N	LEU	636	30.007	64.308	6.721	1.00	54.04
875	CA	LEU	636	30.756	64.222	7.970	1.00	54.00
876	C	LEU	636	31.118	62.774	8.280	1.00	52.73
877	O	LEU	636	30.238	61.939	8.474	1.00	52.98
878	CB	LEU	636	30.018	64.862	9.170	1.00	61.18
879	CG	LEU	636	30.886	65.075	10.440	1.00	99.90
880	CD1	LEU	636	31.840	66.285	10.304	1.00	99.90
881	CD2	LEU	636	30.007	65.206	11.701	1.00	99.90
882	N	PRO	637	32.410	62.469	8.330	1.00	47.20
883	CA	PRO	637	32.837	61.103	8.611	1.00	47.93
884	C	PRO	637	32.365	60.555	9.969	1.00	45.20
885	O	PRO	637	32.004	59.376	10.065	1.00	41.96
886	CB	PRO	637	34.365	60.995	8.489	1.00	47.55
887	CG	PRO	637	34.792	62.388	8.982	1.00	99.90
888	CD	PRO	637	33.765	63.328	8.343	1.00	99.90
889	N	CYS	638	32.359	61.394	11.012	1.00	41.56
890	CA	CYS	638	31.923	60.938	12.337	1.00	34.71
891	C	CYS	638	30.419	60.645	12.344	1.00	33.35
892	O	CYS	638	29.985	59.654	12.927	1.00	30.89
893	CB	CYS	638	32.341	61.841	13.519	1.00	36.41
894	SG	CYS	638	31.647	63.515	13.583	1.00	99.90
895	N	MET	639	29.644	61.502	11.684	1.00	32.63
896	CA	MET	639	28.196	61.332	11.615	1.00	35.71
897	C	MET	639	27.821	60.152	10.712	1.00	35.32
898	O	MET	639	26.883	59.415	11.002	1.00	33.54
899	CB	MET	639	27.482	62.566	11.004	1.00	42.64
900	CG	MET	639	25.996	62.404	10.638	1.00	99.90
901	SD	MET	639	25.346	63.899	9.804	1.00	99.90
902	CE	MET	639	24.091	63.111	8.739	1.00	99.90
903	N	TYR	640	28.560	59.979	9.620	1.00	31.90

904	CA	TYR	640	28.315	58.858	8.708	1.00	28.99
905	C	TYR	640	28.560	57.587	9.490	1.00	25.10
906	O	TYR	640	27.802	56.627	9.404	1.00	29.55
907	CB	TYR	640	29.281	58.918	7.518	1.00	37.34
908	CG	TYR	640	29.171	57.750	6.560	1.00	40.29
909	CD1	TYR	640	28.014	57.544	5.805	1.00	40.54
910	CD2	TYR	640	30.233	56.862	6.397	1.00	42.80
911	CE1	TYR	640	27.918	56.487	4.913	1.00	42.21
912	CE2	TYR	640	30.148	55.798	5.504	1.00	45.44
913	CZ	TYR	640	28.988	55.618	4.762	1.00	44.14
914	OH	TYR	640	28.896	54.572	3.871	1.00	48.25
915	N	ASP	641	29.622	57.572	10.282	1.00	24.54
916	CA	ASP	641	29.907	56.378	11.043	1.00	25.44
917	C	ASP	641	28.766	56.107	12.019	1.00	28.08
918	O	ASP	641	28.423	54.954	12.269	1.00	31.55
919	CB	ASP	641	31.224	56.521	11.805	1.00	32.47
920	CG	ASP	641	31.748	55.265	12.517	1.00	99.90
921	OD1	ASP	641	32.268	55.294	13.623	1.00	99.90
922	OD2	ASP	641	31.547	54.123	11.794	1.00	99.90
923	N	GLN	642	28.183	57.165	12.575	1.00	25.12
924	CA	GLN	642	27.081	56.967	13.514	1.00	25.95
925	C	GLN	642	25.853	56.449	12.766	1.00	27.16
926	O	GLN	642	25.099	55.631	13.289	1.00	29.13
927	CB	GLN	642	26.776	58.283	14.226	1.00	32.01
928	CG	GLN	642	25.534	58.198	15.118	1.00	99.90
929	CD	GLN	642	25.367	59.502	15.876	1.00	99.90
930	OE1	GLN	642	25.084	59.490	17.059	1.00	99.90
931	NE2	GLN	642	25.556	60.682	15.111	1.00	99.90
932	N	CYS	643	25.641	56.940	11.549	1.00	26.93
933	CA	CYS	643	24.514	56.484	10.748	1.00	28.14
934	C	CYS	643	24.633	55.008	10.390	1.00	24.65
935	O	CYS	643	23.628	54.295	10.365	1.00	25.73
936	CB	CYS	643	24.377	57.324	9.477	1.00	24.73
937	SG	CYS	643	23.765	59.023	9.748	1.00	32.75
938	N	LYS	644	25.853	54.544	10.110	1.00	25.25
939	CA	LYS	644	26.062	53.132	9.792	1.00	26.29
940	C	LYS	644	25.682	52.271	10.978	1.00	27.01
941	O	LYS	644	25.217	51.133	10.827	1.00	27.73
942	CB	LYS	644	27.522	52.862	9.434	1.00	28.72
943	CG	LYS	644	27.792	51.395	9.014	1.00	99.90
944	CD	LYS	644	29.258	51.072	8.711	1.00	99.90
945	CE	LYS	644	29.388	49.579	8.381	1.00	99.90
946	NZ	LYS	644	30.760	49.297	7.922	1.00	99.90
947	N	HIS	645	25.914	52.808	12.169	1.00	28.68
948	CA	HIS	645	25.574	52.111	13.399	1.00	27.55
949	C	HIS	645	24.058	52.056	13.507	1.00	20.19
950	O	HIS	645	23.490	51.021	13.856	1.00	28.87
951	CB	HIS	645	26.107	52.749	14.715	1.00	37.30

952	CG	HIS	645	27.612	52.692	14.796	1.00	99.90
953	ND1	HIS	645	28.464	52.435	13.772	1.00	99.90
954	CD2	HIS	645	28.375	52.877	15.984	1.00	99.90
955	CE1	HIS	645	29.707	52.477	14.312	1.00	99.90
956	NE2	HIS	645	29.741	52.753	15.701	1.00	99.90
957	N	MET	646	23.410	53.174	13.213	1.00	20.28
958	CA	MET	646	21.953	53.226	13.270	1.00	23.80
959	C	MET	646	21.364	52.299	12.209	1.00	25.24
960	O	MET	646	20.358	51.634	12.444	1.00	23.42
961	CB	MET	646	21.457	54.660	13.040	1.00	23.19
962	CG	MET	646	21.841	55.620	14.177	1.00	25.74
963	SD	MET	646	21.014	57.221	13.996	1.00	29.64
964	CE	MET	646	21.961	57.963	12.711	1.00	40.66
965	N	LEU	647	22.017	52.247	11.053	1.00	27.17
966	CA	LEU	647	21.560	51.430	9.929	1.00	27.11
967	C	LEU	647	21.425	49.945	10.251	1.00	28.77
968	O	LEU	647	20.705	49.207	9.571	1.00	26.96
969	CB	LEU	647	22.502	51.592	8.740	1.00	27.64
970	CG	LEU	647	22.725	53.021	8.174	1.00	99.90
971	CD1	LEU	647	23.610	52.959	6.921	1.00	99.90
972	CD2	LEU	647	21.407	53.741	7.842	1.00	99.90
973	N	TYR	648	22.122	49.506	11.291	1.00	27.01
974	CA	TYR	648	22.068	48.111	11.700	1.00	29.15
975	C	TYR	648	20.655	47.659	12.025	1.00	27.44
976	O	TYR	648	20.301	46.504	11.793	1.00	26.00
977	CB	TYR	648	22.937	47.884	12.928	1.00	27.84
978	CG	TYR	648	24.436	48.162	12.771	1.00	99.90
979	CD1	TYR	648	24.976	49.355	13.263	1.00	99.90
980	CD2	TYR	648	25.270	47.239	12.134	1.00	99.90
981	CE1	TYR	648	26.333	49.624	13.113	1.00	99.90
982	CE2	TYR	648	26.628	47.512	11.984	1.00	99.90
983	CZ	TYR	648	27.158	48.702	12.474	1.00	99.90
984	OH	TYR	648	28.490	48.967	12.323	1.00	99.90
985	N	VAL	649	19.852	48.556	12.584	1.00	23.42
986	CA	VAL	649	18.493	48.186	12.934	1.00	25.19
987	C	VAL	649	17.612	47.883	11.712	1.00	22.21
988	O	VAL	649	17.038	46.798	11.627	1.00	28.86
989	CB	VAL	649	17.786	49.291	13.791	1.00	25.31
990	CG1	VAL	649	18.566	49.652	15.080	1.00	99.90
991	CG2	VAL	649	16.350	48.878	14.193	1.00	99.90
992	N	SER	650	17.484	48.821	10.756	1.00	22.89
993	CA	SER	650	16.645	48.538	9.576	1.00	26.67
994	C	SER	650	17.123	47.268	8.877	1.00	25.60
995	O	SER	650	16.329	46.505	8.316	1.00	25.13
996	CB	SER	650	16.871	49.767	8.690	1.00	22.17
997	OG	SER	650	18.194	49.823	8.144	1.00	99.90
998	N	SER	651	18.438	47.055	8.909	1.00	29.12
999	CA	SER	651	19.039	45.877	8.287	1.00	28.65

1000	C	SER	651	18.555	44.601	8.929	1.00	30.22
1001	O	SER	651	18.250	43.641	8.228	1.00	28.51
1002	CB	SER	651	20.571	45.944	8.347	1.00	33.89
1003	OG	SER	651	21.083	45.792	9.676	1.00	99.90
1004	N	GLU	652	18.477	44.579	10.256	1.00	25.11
1005	CA	GLU	652	17.997	43.392	10.939	1.00	25.25
1006	C	GLU	652	16.513	43.250	10.723	1.00	21.49
1007	O	GLU	652	16.022	42.128	10.673	1.00	25.66
1008	CB	GLU	652	18.332	43.429	12.437	1.00	28.40
1009	CG	GLU	652	19.812	43.255	12.685	1.00	41.59
1010	CD	GLU	652	20.311	41.886	12.215	1.00	49.95
1011	OE1	GLU	652	19.494	40.940	12.148	1.00	44.78
1012	OE2	GLU	652	21.523	41.746	11.929	1.00	51.07
1013	N	LEU	653	15.810	44.381	10.587	1.00	24.33
1014	CA	LEU	653	14.366	44.377	10.349	1.00	26.06
1015	C	LEU	653	14.098	43.720	9.012	1.00	26.07
1016	O	LEU	653	13.183	42.919	8.888	1.00	22.03
1017	CB	LEU	653	13.777	45.803	10.351	1.00	22.64
1018	CG	LEU	653	13.974	46.674	11.621	1.00	99.90
1019	CD1	LEU	653	13.225	48.005	11.469	1.00	99.90
1020	CD2	LEU	653	13.515	45.964	12.905	1.00	99.90
1021	N	HIS	654	14.917	44.058	8.021	1.00	26.08
1022	CA	HIS	654	14.784	43.475	6.679	1.00	24.64
1023	C	HIS	654	15.102	41.986	6.716	1.00	26.29
1024	O	HIS	654	14.350	41.166	6.183	1.00	28.56
1025	CB	HIS	654	15.741	44.168	5.693	1.00	28.11
1026	CG	HIS	654	15.011	44.831	4.562	1.00	99.90
1027	ND1	HIS	654	13.630	44.845	4.380	1.00	99.90
1028	CD2	HIS	654	15.664	45.519	3.549	1.00	99.90
1029	CE1	HIS	654	13.555	45.565	3.245	1.00	99.90
1030	NE2	HIS	654	14.716	46.000	2.684	1.00	99.90
1031	N	ARG	655	16.215	41.635	7.356	1.00	22.16
1032	CA	ARG	655	16.655	40.248	7.453	1.00	28.14
1033	C	ARG	655	15.632	39.355	8.165	1.00	29.30
1034	O	ARG	655	15.288	38.265	7.691	1.00	29.13
1035	CB	ARG	655	18.000	40.212	8.187	1.00	31.67
1036	CG	ARG	655	18.709	38.870	8.246	1.00	41.13
1037	CD	ARG	655	19.991	38.988	9.093	1.00	46.76
1038	NE	ARG	655	20.696	37.673	9.123	1.00	99.90
1039	CZ	ARG	655	21.836	37.426	9.761	1.00	99.90
1040	NH1	ARG	655	22.334	36.232	9.690	1.00	99.90
1041	NH2	ARG	655	22.482	38.320	10.456	1.00	99.90
1042	N	LEU	656	15.137	39.816	9.305	1.00	29.04
1043	CA	LEU	656	14.166	39.042	10.067	1.00	27.03
1044	C	LEU	656	12.717	39.206	9.606	1.00	24.56
1045	O	LEU	656	11.843	38.435	10.014	1.00	25.98
1046	CB	LEU	656	14.250	39.420	11.556	1.00	30.03
1047	CG	LEU	656	15.510	39.055	12.345	1.00	36.08

1048	CD1	LEU	656	15.367	39.505	13.786	1.00	28.22
1049	CD2	LEU	656	15.715	37.556	12.295	1.00	33.46
1050	N	GLN	657	12.466	40.202	8.760	1.00	24.63
1051	CA	GLN	657	11.116	40.499	8.294	1.00	24.29
1052	C	GLN	657	10.156	40.706	9.479	1.00	28.28
1053	O	GLN	657	9.089	40.084	9.572	1.00	26.02
1054	CB	GLN	657	10.603	39.400	7.354	1.00	31.81
1055	CG	GLN	657	11.444	39.296	6.098	1.00	34.45
1056	CD	GLN	657	10.824	38.430	5.002	1.00	43.12
1057	OE1	GLN	657	11.432	38.232	3.941	1.00	48.46
1058	NE2	GLN	657	9.566	37.825	5.223	1.00	38.30
1059	N	VAL	658	10.561	41.594	10.384	1.00	23.00
1060	CA	VAL	658	9.762	41.941	11.568	1.00	23.27
1061	C	VAL	658	8.393	42.492	11.169	1.00	20.62
1062	O	VAL	658	8.270	43.299	10.243	1.00	24.25
1063	CB	VAL	658	10.506	42.989	12.436	1.00	22.34
1064	CG1	VAL	658	9.623	43.484	13.580	1.00	22.21
1065	CG2	VAL	658	11.756	42.374	12.981	1.00	20.16
1066	N	SER	659	7.358	42.043	11.871	1.00	21.62
1067	CA	SER	659	6.014	42.485	11.562	1.00	22.92
1068	C	SER	659	5.624	43.697	12.393	1.00	21.08
1069	O	SER	659	6.230	43.974	13.424	1.00	22.56
1070	CB	SER	659	5.014	41.364	11.837	1.00	23.84
1071	OG	SER	659	4.896	41.029	13.214	1.00	27.14
1072	N	TYR	660	4.616	44.417	11.921	1.00	22.79
1073	CA	TYR	660	4.110	45.589	12.619	1.00	26.53
1074	C	TYR	660	3.729	45.186	14.046	1.00	24.03
1075	O	TYR	660	4.017	45.904	14.994	1.00	23.00
1076	CB	TYR	660	2.883	46.138	11.863	1.00	26.89
1077	CG	TYR	660	3.117	46.616	10.426	1.00	99.90
1078	CD1	TYR	660	2.748	45.797	9.353	1.00	99.90
1079	CD2	TYR	660	3.703	47.859	10.174	1.00	99.90
1080	CE1	TYR	660	2.970	46.214	8.044	1.00	99.90
1081	CE2	TYR	660	3.924	48.275	8.863	1.00	99.90
1082	CZ	TYR	660	3.557	47.453	7.801	1.00	99.90
1083	OH	TYR	660	3.778	47.863	6.516	1.00	99.90
1084	N	GLU	661	3.096	44.023	14.191	1.00	24.42
1085	CA	GLU	661	2.660	43.541	15.509	1.00	24.69
1086	C	GLU	661	3.838	43.258	16.431	1.00	21.73
1087	O	GLU	661	3.771	43.539	17.622	1.00	23.19
1088	CB	GLU	661	1.819	42.269	15.378	1.00	27.58
1089	CG	GLU	661	0.536	42.386	14.563	1.00	32.90
1090	CD	GLU	661	0.776	42.657	13.079	1.00	38.95
1091	OE1	GLU	661	1.753	42.130	12.509	1.00	36.30
1092	OE2	GLU	661	-0.044	43.378	12.472	1.00	49.03
1093	N	GLU	662	4.911	42.676	15.890	1.00	21.48
1094	CA	GLU	662	6.097	42.398	16.697	1.00	20.83
1095	C	GLU	662	6.795	43.702	17.061	1.00	20.85

1096	O	GLU	662	7.246	43.876	18.182	1.00	23.00
1097	CB	GLU	662	7.090	41.515	15.936	1.00	22.67
1098	CG	GLU	662	6.640	40.056	15.739	1.00	25.39
1099	CD	GLU	662	7.482	39.316	14.703	1.00	33.69
1100	OE1	GLU	662	8.114	39.980	13.843	1.00	30.03
1101	OE2	GLU	662	7.506	38.070	14.732	1.00	30.51
1102	N	TYR	663	6.916	44.604	16.093	1.00	21.31
1103	CA	TYR	663	7.573	45.888	16.342	1.00	22.08
1104	C	TYR	663	6.893	46.682	17.474	1.00	21.29
1105	O	TYR	663	7.564	47.277	18.327	1.00	20.03
1106	CB	TYR	663	7.540	46.721	15.070	1.00	23.06
1107	CG	TYR	663	7.851	48.167	15.290	1.00	22.01
1108	CD1	TYR	663	9.155	48.583	15.542	1.00	22.32
1109	CD2	TYR	663	6.831	49.110	15.260	1.00	23.62
1110	CE1	TYR	663	9.434	49.925	15.755	1.00	27.65
1111	CE2	TYR	663	7.101	50.458	15.474	1.00	28.88
1112	CZ	TYR	663	8.402	50.863	15.722	1.00	22.16
1113	OH	TYR	663	8.673	52.185	15.935	1.00	99.90
1114	N	LEU	664	5.567	46.711	17.455	1.00	21.31
1115	CA	LEU	664	4.806	47.451	18.468	1.00	23.49
1116	C	LEU	664	5.083	46.979	19.900	1.00	26.91
1117	O	LEU	664	5.233	47.802	20.808	1.00	20.81
1118	CB	LEU	664	3.310	47.384	18.143	1.00	24.50
1119	CG	LEU	664	2.922	48.148	16.864	1.00	23.57
1120	CD1	LEU	664	1.452	47.937	16.521	1.00	22.54
1121	CD2	LEU	664	3.191	49.647	17.087	1.00	27.51
1122	N	CYS	665	5.147	45.662	20.101	1.00	22.87
1123	CA	CYS	665	5.431	45.097	21.416	1.00	26.80
1124	C	CYS	665	6.902	45.304	21.783	1.00	25.96
1125	O	CYS	665	7.240	45.589	22.934	1.00	20.10
1126	CB	CYS	665	5.124	43.601	21.428	1.00	27.46
1127	SG	CYS	665	3.371	43.221	21.079	1.00	33.20
1128	N	MET	666	7.789	45.143	20.810	1.00	18.27
1129	CA	MET	666	9.187	45.349	21.107	1.00	20.73
1130	C	MET	666	9.446	46.800	21.523	1.00	18.21
1131	O	MET	666	10.282	47.056	22.376	1.00	20.04
1132	CB	MET	666	10.033	44.979	19.899	1.00	23.28
1133	CG	MET	666	9.931	43.517	19.514	1.00	26.12
1134	SD	MET	666	10.766	43.239	17.916	1.00	30.71
1135	CE	MET	666	12.364	43.447	18.420	1.00	17.04
1136	N	LYS	667	8.730	47.750	20.934	1.00	22.26
1137	CA	LYS	667	8.958	49.158	21.285	1.00	21.99
1138	C	LYS	667	8.593	49.432	22.742	1.00	23.71
1139	O	LYS	667	9.255	50.224	23.423	1.00	20.06
1140	CB	LYS	667	8.175	50.091	20.342	1.00	24.02
1141	CG	LYS	667	8.621	51.548	20.407	1.00	31.07
1142	CD	LYS	667	8.217	52.309	19.139	1.00	38.28
1143	CE	LYS	667	6.708	52.411	18.956	1.00	39.48

1144	NZ	LYS	667	5.961	53.284	19.944	1.00	42.42
1145	N	THR	668	7.549	48.768	23.231	1.00	20.18
1146	CA	THR	668	7.158	48.951	24.623	1.00	19.22
1147	C	THR	668	8.223	48.345	25.523	1.00	21.84
1148	O	THR	668	8.587	48.917	26.548	1.00	21.05
1149	CB	THR	668	5.822	48.260	24.936	1.00	19.35
1150	OG1	THR	668	4.778	48.814	24.146	1.00	99.90
1151	CG2	THR	668	5.314	48.380	26.389	1.00	99.90
1152	N	LEU	669	8.733	47.181	25.140	1.00	19.81
1153	CA	LEU	669	9.769	46.539	25.937	1.00	20.73
1154	C	LEU	669	11.013	47.417	26.009	1.00	24.51
1155	O	LEU	669	11.743	47.380	26.999	1.00	21.96
1156	CB	LEU	669	10.104	45.149	25.370	1.00	21.13
1157	CG	LEU	669	8.943	44.165	25.568	1.00	20.69
1158	CD1	LEU	669	9.239	42.871	24.849	1.00	23.72
1159	CD2	LEU	669	8.725	43.908	27.077	1.00	21.59
1160	N	LEU	670	11.252	48.224	24.980	1.00	22.43
1161	CA	LEU	670	12.400	49.122	25.007	1.00	24.57
1162	C	LEU	670	12.195	50.225	26.025	1.00	22.02
1163	O	LEU	670	13.144	50.636	26.677	1.00	23.56
1164	CB	LEU	670	12.663	49.769	23.650	1.00	19.15
1165	CG	LEU	670	13.473	49.023	22.615	1.00	31.93
1166	CD1	LEU	670	13.732	50.001	21.470	1.00	28.38
1167	CD2	LEU	670	14.807	48.532	23.219	1.00	26.52
1168	N	LEU	671	10.962	50.710	26.138	1.00	18.07
1169	CA	LEU	671	10.629	51.743	27.114	1.00	20.16
1170	C	LEU	671	10.919	51.217	28.524	1.00	23.85
1171	O	LEU	671	11.313	51.963	29.427	1.00	23.95
1172	CB	LEU	671	9.144	52.087	27.013	1.00	21.07
1173	CG	LEU	671	8.548	52.995	28.099	1.00	22.15
1174	CD1	LEU	671	9.240	54.359	28.086	1.00	21.62
1175	CD2	LEU	671	7.050	53.150	27.871	1.00	22.53
1176	N	LEU	672	10.721	49.917	28.697	1.00	16.99
1177	CA	LEU	672	10.891	49.261	29.979	1.00	21.87
1178	C	LEU	672	12.190	48.477	30.038	1.00	24.10
1179	O	LEU	672	12.282	47.519	30.799	1.00	24.64
1180	CB	LEU	672	9.721	48.283	30.185	1.00	20.22
1181	CG	LEU	672	8.317	48.845	29.941	1.00	27.92
1182	CD1	LEU	672	7.264	47.732	30.054	1.00	24.44
1183	CD2	LEU	672	8.030	49.964	30.943	1.00	21.00
1184	N	SER	673	13.210	48.881	29.281	1.00	21.55
1185	CA	SER	673	14.431	48.072	29.246	1.00	26.34
1186	C	SER	673	15.616	48.473	30.129	1.00	21.48
1187	O	SER	673	16.654	47.815	30.120	1.00	25.22
1188	CB	SER	673	14.882	47.946	27.792	1.00	24.75
1189	OG	SER	673	15.366	49.181	27.251	1.00	99.90
1190	N	SER	674	15.446	49.532	30.903	1.00	20.94
1191	CA	SER	674	16.501	50.026	31.780	1.00	23.18

1192	C	SER	674	15.855	50.647	33.002	1.00	24.51
1193	O	SER	674	14.884	51.395	32.875	1.00	20.61
1194	CB	SER	674	17.349	51.117	31.062	1.00	27.14
1195	OG	SER	674	16.627	52.336	30.852	1.00	99.90
1196	N	VAL	675	16.377	50.324	34.183	1.00	23.20
1197	CA	VAL	675	15.853	50.899	35.422	1.00	22.29
1198	C	VAL	675	17.003	51.371	36.308	1.00	23.93
1199	O	VAL	675	18.163	51.045	36.053	1.00	23.93
1200	CB	VAL	675	14.995	49.884	36.192	1.00	24.86
1201	CG1	VAL	675	13.702	49.465	35.450	1.00	99.90
1202	CG2	VAL	675	14.532	50.309	37.613	1.00	99.90
1203	N	PRO	676	16.699	52.154	37.350	1.00	23.63
1204	CA	PRO	676	17.741	52.651	38.250	1.00	26.05
1205	C	PRO	676	18.406	51.512	39.004	1.00	30.91
1206	O	PRO	676	17.822	50.433	39.164	1.00	27.25
1207	CB	PRO	676	16.969	53.583	39.189	1.00	28.62
1208	CG	PRO	676	15.761	54.002	38.335	1.00	25.78
1209	CD	PRO	676	15.387	52.647	37.791	1.00	28.72
1210	N	LYS	677	19.632	51.754	39.460	1.00	31.80
1211	CA	LYS	677	20.378	50.754	40.215	1.00	34.58
1212	C	LYS	677	19.609	50.311	41.453	1.00	32.37
1213	O	LYS	677	19.708	49.157	41.871	1.00	38.50
1214	CB	LYS	677	21.745	51.314	40.633	1.00	34.68
1215	CG	LYS	677	22.631	50.283	41.377	1.00	99.90
1216	CD	LYS	677	23.976	50.826	41.868	1.00	99.90
1217	CE	LYS	677	24.713	49.726	42.643	1.00	99.90
1218	NZ	LYS	677	26.075	50.184	42.968	1.00	99.90
1219	N	ASP	678	18.837	51.223	42.031	1.00	33.46
1220	CA	ASP	678	18.058	50.899	43.219	1.00	35.43
1221	C	ASP	678	16.645	50.442	42.859	1.00	37.02
1222	O	ASP	678	15.809	50.203	43.734	1.00	34.87
1223	CB	ASP	678	18.002	52.103	44.174	1.00	40.38
1224	CG	ASP	678	17.367	51.860	45.551	1.00	99.90
1225	OD1	ASP	678	16.636	52.671	46.100	1.00	99.90
1226	OD2	ASP	678	17.688	50.639	46.076	1.00	99.90
1227	N	GLY	679	16.380	50.302	41.565	1.00	32.49
1228	CA	GLY	679	15.063	49.872	41.144	1.00	28.49
1229	C	GLY	679	14.103	51.045	41.110	1.00	30.77
1230	O	GLY	679	14.481	52.171	41.415	1.00	29.05
1231	N	LEU	680	12.857	50.766	40.745	1.00	27.80
1232	CA	LEU	680	11.812	51.772	40.643	1.00	31.88
1233	C	LEU	680	10.938	51.781	41.896	1.00	30.49
1234	O	LEU	680	10.871	50.788	42.614	1.00	28.71
1235	CB	LEU	680	10.929	51.449	39.440	1.00	28.43
1236	CG	LEU	680	11.569	51.477	38.052	1.00	31.10
1237	CD1	LEU	680	10.606	50.863	37.058	1.00	29.92
1238	CD2	LEU	680	11.928	52.921	37.667	1.00	27.76
1239	N	LYS	681	10.251	52.892	42.141	1.00	33.09

1240	CA	LYS	681	9.359	52.979	43.300	1.00	33.34
1241	C	LYS	681	8.216	51.968	43.117	1.00	37.41
1242	O	LYS	681	7.767	51.323	44.075	1.00	35.58
1243	CB	LYS	681	8.779	54.391	43.419	1.00	37.62
1244	CG	LYS	681	9.834	55.481	43.433	1.00	43.12
1245	CD	LYS	681	9.273	56.849	43.827	1.00	55.06
1246	CE	LYS	681	10.419	57.868	43.884	1.00	99.90
1247	NZ	LYS	681	9.864	59.218	44.093	1.00	99.90
1248	N	SER	682	7.734	51.854	41.880	1.00	28.39
1249	CA	SER	682	6.667	50.925	41.537	1.00	29.00
1250	C	SER	682	7.282	49.701	40.864	1.00	30.23
1251	O	SER	682	6.865	49.312	39.778	1.00	26.81
1252	CB	SER	682	5.678	51.594	40.578	1.00	23.84
1253	OG	SER	682	4.977	52.693	41.139	1.00	31.90
1254	N	GLN	683	8.273	49.089	41.508	1.00	29.41
1255	CA	GLN	683	8.936	47.936	40.910	1.00	28.12
1256	C	GLN	683	7.980	46.776	40.638	1.00	30.39
1257	O	GLN	683	8.040	46.157	39.582	1.00	26.03
1258	CB	GLN	683	10.088	47.471	41.801	1.00	25.64
1259	CG	GLN	683	11.048	46.487	41.154	1.00	32.23
1260	CD	GLN	683	11.776	47.082	39.957	1.00	37.10
1261	OE1	GLN	683	12.179	48.247	39.972	1.00	37.64
1262	NE2	GLN	683	12.010	46.204	38.875	1.00	42.95
1263	N	GLU	684	7.107	46.462	41.592	1.00	27.88
1264	CA	GLU	684	6.155	45.374	41.386	1.00	30.26
1265	C	GLU	684	5.275	45.594	40.169	1.00	27.76
1266	O	GLU	684	5.134	44.699	39.332	1.00	28.54
1267	CB	GLU	684	5.237	45.203	42.590	1.00	31.84
1268	CG	GLU	684	4.246	46.371	42.908	1.00	99.90
1269	CD	GLU	684	3.384	46.270	44.169	1.00	99.90
1270	OE1	GLU	684	2.605	47.147	44.516	1.00	99.90
1271	OE2	GLU	684	3.567	45.114	44.867	1.00	99.90
1272	N	LEU	685	4.674	46.779	40.087	1.00	27.40
1273	CA	LEU	685	3.816	47.129	38.965	1.00	27.76
1274	C	LEU	685	4.627	47.085	37.676	1.00	27.08
1275	O	LEU	685	4.134	46.647	36.636	1.00	24.43
1276	CB	LEU	685	3.232	48.527	39.136	1.00	29.57
1277	CG	LEU	685	2.395	48.818	40.411	1.00	99.90
1278	CD1	LEU	685	1.806	50.235	40.343	1.00	99.90
1279	CD2	LEU	685	1.265	47.798	40.626	1.00	99.90
1280	N	PHE	686	5.875	47.527	37.758	1.00	25.08
1281	CA	PHE	686	6.751	47.536	36.586	1.00	25.20
1282	C	PHE	686	7.026	46.127	36.084	1.00	22.17
1283	O	PHE	686	6.972	45.868	34.879	1.00	24.69
1284	CB	PHE	686	8.060	48.268	36.910	1.00	24.39
1285	CG	PHE	686	9.148	48.066	35.883	1.00	25.18
1286	CD1	PHE	686	9.213	48.875	34.740	1.00	26.95
1287	CD2	PHE	686	10.079	47.041	36.029	1.00	21.90

1288	CE1	PHE	686	10.198	48.660	33.756	1.00	22.61
1289	CE2	PHE	686	11.065	46.812	35.054	1.00	21.56
1290	CZ	PHE	686	11.124	47.622	33.915	1.00	23.75
1291	N	ASP	687	7.312	45.216	37.004	1.00	26.80
1292	CA	ASP	687	7.573	43.819	36.640	1.00	30.80
1293	C	ASP	687	6.365	43.212	35.929	1.00	27.28
1294	O	ASP	687	6.498	42.543	34.905	1.00	27.77
1295	CB	ASP	687	7.859	42.979	37.890	1.00	28.70
1296	CG	ASP	687	8.326	41.535	37.658	1.00	99.90
1297	OD1	ASP	687	7.948	40.595	38.342	1.00	99.90
1298	OD2	ASP	687	9.181	41.418	36.599	1.00	99.90
1299	N	GLU	688	5.188	43.418	36.505	1.00	29.50
1300	CA	GLU	688	3.961	42.897	35.922	1.00	27.52
1301	C	GLU	688	3.731	43.493	34.533	1.00	29.29
1302	O	GLU	688	3.318	42.805	33.610	1.00	29.26
1303	CB	GLU	688	2.762	43.210	36.826	1.00	32.59
1304	CG	GLU	688	2.653	42.336	38.078	1.00	38.26
1305	CD	GLU	688	1.528	42.774	39.012	1.00	47.34
1306	OE1	GLU	688	0.440	43.140	38.517	1.00	51.54
1307	OE2	GLU	688	1.720	42.734	40.248	1.00	49.88
1308	N	ILE	689	4.007	44.777	34.381	1.00	25.95
1309	CA	ILE	689	3.803	45.408	33.093	1.00	26.70
1310	C	ILE	689	4.737	44.798	32.059	1.00	26.41
1311	O	ILE	689	4.317	44.414	30.966	1.00	25.61
1312	CB	ILE	689	4.044	46.907	33.209	1.00	26.67
1313	CG2	ILE	689	3.757	47.671	31.880	1.00	99.90
1314	CG1	ILE	689	3.246	47.608	34.354	1.00	99.90
1315	CD1	ILE	689	3.697	49.040	34.711	1.00	99.90
1316	N	ARG	690	6.007	44.684	32.422	1.00	26.84
1317	CA	ARG	690	6.989	44.124	31.515	1.00	29.65
1318	C	ARG	690	6.600	42.691	31.106	1.00	31.46
1319	O	ARG	690	6.645	42.341	29.931	1.00	28.49
1320	CB	ARG	690	8.366	44.185	32.177	1.00	29.38
1321	CG	ARG	690	9.522	43.957	31.232	1.00	38.40
1322	CD	ARG	690	10.844	44.337	31.875	1.00	33.58
1323	NE	ARG	690	11.947	44.131	30.940	1.00	43.23
1324	CZ	ARG	690	12.434	42.942	30.613	1.00	45.03
1325	NH1	ARG	690	12.020	41.789	31.215	1.00	58.21
1326	NH2	ARG	690	13.427	42.875	29.683	1.00	52.78
1327	N	MET	691	6.189	41.870	32.066	1.00	29.00
1328	CA	MET	691	5.783	40.497	31.758	1.00	29.23
1329	C	MET	691	4.586	40.447	30.814	1.00	25.05
1330	O	MET	691	4.523	39.601	29.929	1.00	27.74
1331	CB	MET	691	5.456	39.741	33.047	1.00	29.17
1332	CG	MET	691	6.626	39.562	34.038	1.00	99.90
1333	SD	MET	691	6.151	38.415	35.341	1.00	99.90
1334	CE	MET	691	7.506	38.731	36.480	1.00	99.90
1335	N	THR	692	3.631	41.346	31.015	1.00	27.46

1336	CA	THR	692	2.445	41.405	30.170	1.00	26.94
1337	C	THR	692	2.837	41.701	28.727	1.00	28.69
1338	O	THR	692	2.275	41.136	27.797	1.00	24.01
1339	CB	THR	692	1.488	42.485	30.676	1.00	33.23
1340	OG1	THR	692	1.053	42.187	31.996	1.00	99.90
1341	CG2	THR	692	0.183	42.674	29.872	1.00	99.90
1342	N	TYR	693	3.799	42.594	28.538	1.00	23.69
1343	CA	TYR	693	4.232	42.918	27.185	1.00	24.43
1344	C	TYR	693	5.124	41.845	26.579	1.00	25.10
1345	O	TYR	693	5.160	41.684	25.364	1.00	24.91
1346	CB	TYR	693	4.888	44.291	27.176	1.00	22.98
1347	CG	TYR	693	3.840	45.374	27.203	1.00	21.21
1348	CD1	TYR	693	3.165	45.732	26.032	1.00	21.26
1349	CD2	TYR	693	3.489	46.007	28.393	1.00	21.12
1350	CE1	TYR	693	2.165	46.700	26.038	1.00	22.44
1351	CE2	TYR	693	2.487	46.979	28.411	1.00	23.86
1352	CZ	TYR	693	1.829	47.325	27.225	1.00	28.65
1353	OH	TYR	693	0.884	48.311	27.226	1.00	23.47
1354	N	ILE	694	5.835	41.101	27.415	1.00	23.21
1355	CA	ILE	694	6.650	40.015	26.901	1.00	29.14
1356	C	ILE	694	5.653	38.965	26.405	1.00	30.21
1357	O	ILE	694	5.832	38.363	25.350	1.00	26.87
1358	CB	ILE	694	7.584	39.430	28.003	1.00	29.35
1359	CG1	ILE	694	8.690	40.443	28.327	1.00	23.92
1360	CG2	ILE	694	8.219	38.114	27.542	1.00	27.00
1361	CD1	ILE	694	9.626	39.992	29.412	1.00	22.76
1362	N	LYS	695	4.577	38.764	27.154	1.00	28.71
1363	CA	LYS	695	3.580	37.801	26.724	1.00	32.10
1364	C	LYS	695	2.890	38.286	25.458	1.00	29.94
1365	O	LYS	695	2.487	37.489	24.621	1.00	28.11
1366	CB	LYS	695	2.522	37.554	27.805	1.00	35.86
1367	CG	LYS	695	3.015	36.798	29.026	1.00	40.68
1368	CD	LYS	695	1.838	36.332	29.882	1.00	46.12
1369	CE	LYS	695	2.368	35.511	31.065	1.00	99.90
1370	NZ	LYS	695	1.257	35.206	31.985	1.00	99.90
1371	N	GLU	696	2.754	39.596	25.307	1.00	26.26
1372	CA	GLU	696	2.094	40.106	24.118	1.00	24.07
1373	C	GLU	696	2.995	39.939	22.890	1.00	25.19
1374	O	GLU	696	2.502	39.675	21.789	1.00	27.72
1375	CB	GLU	696	1.691	41.569	24.316	1.00	29.75
1376	CG	GLU	696	0.566	42.010	23.401	1.00	32.34
1377	CD	GLU	696	-0.741	41.254	23.669	1.00	48.72
1378	OE1	GLU	696	-0.808	40.500	24.667	1.00	47.00
1379	OE2	GLU	696	-1.707	41.419	22.889	1.00	46.97
1380	N	LEU	697	4.306	40.085	23.073	1.00	23.97
1381	CA	LEU	697	5.250	39.893	21.974	1.00	22.66
1382	C	LEU	697	5.147	38.432	21.518	1.00	30.81
1383	O	LEU	697	5.247	38.138	20.329	1.00	24.16

1384	CB	LEU	697	6.684	40.158	22.448	1.00	22.80
1385	CG	LEU	697	7.794	39.746	21.476	1.00	25.24
1386	CD1	LEU	697	7.669	40.557	20.215	1.00	25.51
1387	CD2	LEU	697	9.177	39.940	22.125	1.00	27.39
1388	N	GLY	698	4.980	37.516	22.471	1.00	24.04
1389	CA	GLY	698	4.860	36.103	22.122	1.00	29.31
1390	C	GLY	698	3.637	35.900	21.243	1.00	28.39
1391	O	GLY	698	3.714	35.207	20.229	1.00	28.22
1392	N	LYS	699	2.519	36.528	21.607	1.00	29.91
1393	CA	LYS	699	1.296	36.425	20.808	1.00	27.78
1394	C	LYS	699	1.524	37.002	19.413	1.00	28.75
1395	O	LYS	699	1.047	36.459	18.420	1.00	30.96
1396	CB	LYS	699	0.141	37.175	21.469	1.00	32.36
1397	CG	LYS	699	-0.319	36.605	22.790	1.00	32.65
1398	CD	LYS	699	-1.435	37.474	23.360	1.00	41.08
1399	CE	LYS	699	-1.870	36.970	24.710	1.00	47.72
1400	NZ	LYS	699	-0.742	36.892	25.724	1.00	54.97
1401	N	ALA	700	2.254	38.111	19.334	1.00	25.66
1402	CA	ALA	700	2.515	38.726	18.035	1.00	26.89
1403	C	ALA	700	3.302	37.744	17.175	1.00	25.18
1404	O	ALA	700	3.029	37.591	15.981	1.00	24.74
1405	CB	ALA	700	3.305	40.026	18.206	1.00	22.45
1406	N	ILE	701	4.271	37.081	17.794	1.00	25.69
1407	CA	ILE	701	5.112	36.113	17.088	1.00	28.42
1408	C	ILE	701	4.237	34.945	16.627	1.00	32.00
1409	O	ILE	701	4.394	34.448	15.513	1.00	33.59
1410	CB	ILE	701	6.243	35.612	18.008	1.00	31.03
1411	CG1	ILE	701	7.259	36.743	18.217	1.00	25.53
1412	CG2	ILE	701	6.912	34.369	17.417	1.00	29.18
1413	CD1	ILE	701	8.342	36.413	19.218	1.00	27.39
1414	N	VAL	702	3.311	34.534	17.488	1.00	33.82
1415	CA	VAL	702	2.409	33.440	17.168	1.00	34.58
1416	C	VAL	702	1.484	33.695	15.991	1.00	37.55
1417	O	VAL	702	0.987	32.754	15.368	1.00	37.64
1418	CB	VAL	702	1.584	33.033	18.453	1.00	99.90
1419	CG1	VAL	702	2.450	32.451	19.597	1.00	99.90
1420	CG2	VAL	702	0.440	32.002	18.241	1.00	99.90
1421	N	LYS	703	1.246	34.963	15.675	1.00	33.59
1422	CA	LYS	703	0.379	35.312	14.563	1.00	37.87
1423	C	LYS	703	0.909	34.783	13.231	1.00	42.05
1424	O	LYS	703	0.137	34.548	12.304	1.00	37.32
1425	CB	LYS	703	0.220	36.832	14.468	1.00	35.77
1426	CG	LYS	703	-0.753	37.281	13.349	1.00	99.90
1427	CD	LYS	703	-0.887	38.797	13.181	1.00	99.90
1428	CE	LYS	703	-1.819	39.094	11.999	1.00	99.90
1429	NZ	LYS	703	-2.088	40.542	11.940	1.00	99.90
1430	N	ARG	704	2.223	34.592	13.144	1.00	42.57
1431	CA	ARG	704	2.855	34.129	11.915	1.00	52.08

1432	C	ARG	704	3.857	33.000	12.122	1.00	54.79
1433	O	ARG	704	4.295	32.377	11.153	1.00	58.54
1434	CB	ARG	704	3.553	35.300	11.220	1.00	52.12
1435	CG	ARG	704	2.602	36.399	10.773	1.00	58.32
1436	CD	ARG	704	3.330	37.570	10.125	1.00	61.04
1437	NE	ARG	704	2.381	38.552	9.608	1.00	72.95
1438	CZ	ARG	704	2.717	39.679	8.985	1.00	76.45
1439	NH1	ARG	704	4.016	40.006	8.710	1.00	80.87
1440	NH2	ARG	704	1.724	40.535	8.609	1.00	77.97
1441	N	GLU	705	4.232	32.744	13.373	1.00	60.36
1442	CA	GLU	705	5.173	31.670	13.672	1.00	65.05
1443	C	GLU	705	4.462	30.478	14.296	1.00	67.98
1444	O	GLU	705	4.360	30.349	15.520	1.00	68.79
1445	CB	GLU	705	6.299	32.164	14.581	1.00	64.71
1446	CG	GLU	705	7.176	33.211	13.919	1.00	68.26
1447	CD	GLU	705	7.851	32.703	12.655	1.00	71.18
1448	OE1	GLU	705	8.482	33.467	11.921	1.00	72.78
1449	OE2	GLU	705	7.975	31.348	12.607	1.00	99.90
1450	N	GLY	706	3.967	29.621	13.410	1.00	70.37
1451	CA	GLY	706	3.248	28.405	13.752	1.00	71.87
1452	C	GLY	706	4.084	27.416	14.573	1.00	72.34
1453	O	GLY	706	3.661	26.978	15.646	1.00	71.39
1454	N	ASN	707	5.266	27.069	14.068	1.00	72.03
1455	CA	ASN	707	6.127	26.131	14.769	1.00	72.71
1456	C	ASN	707	6.392	26.503	16.219	1.00	71.15
1457	O	ASN	707	6.651	27.665	16.528	1.00	71.21
1458	CB	ASN	707	7.464	25.970	13.989	1.00	99.90
1459	CG	ASN	707	7.366	25.516	12.528	1.00	99.90
1460	OD1	ASN	707	7.454	26.300	11.595	1.00	99.90
1461	ND2	ASN	707	7.157	24.252	12.275	1.00	99.90
1462	N	SER	708	6.330	25.521	17.110	1.00	70.79
1463	CA	SER	708	6.571	25.759	18.531	1.00	69.40
1464	C	SER	708	8.038	26.104	18.772	1.00	68.93
1465	O	SER	708	8.369	26.841	19.706	1.00	66.12
1466	CB	SER	708	6.215	24.515	19.380	1.00	71.43
1467	OG	SER	708	7.120	23.424	19.176	1.00	99.90
1468	N	SER	709	8.912	25.561	17.929	1.00	65.17
1469	CA	SER	709	10.339	25.819	18.054	1.00	64.59
1470	C	SER	709	10.702	27.013	17.180	1.00	61.44
1471	O	SER	709	11.567	27.811	17.531	1.00	61.24
1472	CB	SER	709	11.177	24.591	17.623	1.00	65.52
1473	OG	SER	709	11.115	24.341	16.214	1.00	99.90
1474	N	GLN	710	10.031	27.128	16.038	1.00	58.29
1475	CA	GLN	710	10.272	28.237	15.129	1.00	52.84
1476	C	GLN	710	9.868	29.527	15.841	1.00	51.66
1477	O	GLN	710	10.538	30.553	15.720	1.00	45.86
1478	CB	GLN	710	9.447	28.068	13.852	1.00	55.37
1479	CG	GLN	710	9.639	29.168	12.755	1.00	99.90

1480	CD	GLN	710	8.801	29.099	11.472	1.00	99.90
1481	OE1	GLN	710	8.894	29.959	10.612	1.00	99.90
1482	NE2	GLN	710	7.952	28.118	11.299	1.00	99.90
1483	N	ASN	711	8.771	29.458	16.586	1.00	44.60
1484	CA	ASN	711	8.278	30.608	17.328	1.00	45.64
1485	C	ASN	711	9.227	30.873	18.485	1.00	44.47
1486	O	ASN	711	9.455	32.018	18.873	1.00	39.29
1487	CB	ASN	711	6.881	30.328	17.879	1.00	45.32
1488	CG	ASN	711	5.799	29.942	16.865	1.00	99.90
1489	OD1	ASN	711	5.455	28.783	16.688	1.00	99.90
1490	ND2	ASN	711	5.242	30.883	16.151	1.00	99.90
1491	N	TRP	712	9.779	29.796	19.029	1.00	43.23
1492	CA	TRP	712	10.708	29.884	20.141	1.00	42.20
1493	C	TRP	712	12.007	30.512	19.655	1.00	41.29
1494	O	TRP	712	12.572	31.386	20.314	1.00	42.13
1495	CB	TRP	712	10.974	28.488	20.708	1.00	43.71
1496	CG	TRP	712	9.763	27.820	21.365	1.00	99.90
1497	CD1	TRP	712	8.899	26.892	20.747	1.00	99.90
1498	CD2	TRP	712	9.234	28.052	22.618	1.00	99.90
1499	NE1	TRP	712	7.834	26.530	21.595	1.00	99.90
1500	CE2	TRP	712	8.064	27.263	22.748	1.00	99.90
1501	CE3	TRP	712	9.649	28.908	23.670	1.00	99.90
1502	CZ2	TRP	712	7.306	27.317	23.938	1.00	99.90
1503	CZ3	TRP	712	8.887	28.939	24.838	1.00	99.90
1504	CH2	TRP	712	7.733	28.153	24.972	1.00	99.90
1505	N	GLN	713	12.482	30.063	18.497	1.00	35.72
1506	CA	GLN	713	13.705	30.607	17.932	1.00	36.75
1507	C	GLN	713	13.471	32.064	17.536	1.00	31.61
1508	O	GLN	713	14.390	32.882	17.555	1.00	34.73
1509	CB	GLN	713	14.140	29.779	16.718	1.00	41.06
1510	CG	GLN	713	14.425	28.316	17.080	1.00	51.40
1511	CD	GLN	713	14.813	27.460	15.891	1.00	56.24
1512	OE1	GLN	713	15.833	27.698	15.240	1.00	66.21
1513	NE2	GLN	713	13.872	26.543	15.379	1.00	61.83
1514	N	ARG	714	12.228	32.377	17.194	1.00	30.91
1515	CA	ARG	714	11.838	33.731	16.791	1.00	33.76
1516	C	ARG	714	11.909	34.647	18.007	1.00	29.74
1517	O	ARG	714	12.398	35.776	17.934	1.00	28.46
1518	CB	ARG	714	10.410	33.710	16.264	1.00	31.23
1519	CG	ARG	714	9.875	35.044	15.774	1.00	40.84
1520	CD	ARG	714	10.660	35.529	14.587	1.00	36.78
1521	NE	ARG	714	10.044	36.692	13.951	1.00	41.13
1522	CZ	ARG	714	10.522	37.255	12.851	1.00	35.24
1523	NH1	ARG	714	11.641	36.755	12.245	1.00	32.73
1524	NH2	ARG	714	9.876	38.307	12.292	1.00	33.12
1525	N	PHE	715	11.410	34.140	19.125	1.00	27.87
1526	CA	PHE	715	11.411	34.896	20.360	1.00	29.28
1527	C	PHE	715	12.853	35.180	20.724	1.00	30.03

1528	O	PHE	715	13.198	36.292	21.131	1.00	29.75
1529	CB	PHE	715	10.742	34.102	21.471	1.00	30.24
1530	CG	PHE	715	10.605	34.864	22.757	1.00	32.22
1531	CD1	PHE	715	9.640	35.859	22.893	1.00	30.59
1532	CD2	PHE	715	11.446	34.593	23.829	1.00	33.43
1533	CE1	PHE	715	9.515	36.573	24.083	1.00	29.82
1534	CE2	PHE	715	11.330	35.300	25.020	1.00	33.14
1535	CZ	PHE	715	10.360	36.294	25.147	1.00	28.67
1536	N	TYR	716	13.709	34.180	20.544	1.00	28.46
1537	CA	TYR	716	15.123	34.343	20.860	1.00	33.75
1538	C	TYR	716	15.764	35.435	20.016	1.00	30.34
1539	O	TYR	716	16.500	36.271	20.534	1.00	31.44
1540	CB	TYR	716	15.905	33.043	20.630	1.00	32.68
1541	CG	TYR	716	17.391	33.207	20.872	1.00	39.92
1542	CD1	TYR	716	17.904	33.299	22.163	1.00	45.08
1543	CD2	TYR	716	18.278	33.335	19.805	1.00	45.67
1544	CE1	TYR	716	19.270	33.517	22.389	1.00	52.13
1545	CE2	TYR	716	19.643	33.556	20.017	1.00	51.47
1546	CZ	TYR	716	20.131	33.646	21.308	1.00	51.04
1547	OH	TYR	716	21.474	33.869	21.525	1.00	54.66
1548	N	GLN	717	15.487	35.410	18.717	1.00	27.62
1549	CA	GLN	717	16.038	36.383	17.792	1.00	28.60
1550	C	GLN	717	15.598	37.812	18.104	1.00	30.83
1551	O	GLN	717	16.418	38.742	18.128	1.00	26.66
1552	CB	GLN	717	15.619	36.045	16.365	1.00	34.35
1553	CG	GLN	717	16.070	34.670	15.891	1.00	38.32
1554	CD	GLN	717	15.625	34.389	14.474	1.00	43.83
1555	OE1	GLN	717	14.434	34.436	14.160	1.00	44.13
1556	NE2	GLN	717	16.629	34.027	13.543	1.00	49.31
1557	N	LEU	718	14.303	37.983	18.334	1.00	26.84
1558	CA	LEU	718	13.774	39.309	18.625	1.00	25.39
1559	C	LEU	718	14.288	39.865	19.949	1.00	27.79
1560	O	LEU	718	14.634	41.050	20.032	1.00	27.31
1561	CB	LEU	718	12.242	39.283	18.616	1.00	24.65
1562	CG	LEU	718	11.635	38.865	17.267	1.00	26.51
1563	CD1	LEU	718	10.131	38.939	17.303	1.00	29.15
1564	CD2	LEU	718	12.187	39.757	16.171	1.00	24.41
1565	N	THR	719	14.346	39.025	20.979	1.00	26.19
1566	CA	THR	719	14.824	39.484	22.274	1.00	29.70
1567	C	THR	719	16.339	39.696	22.245	1.00	32.67
1568	O	THR	719	16.878	40.522	22.992	1.00	30.17
1569	CB	THR	719	14.411	38.513	23.424	1.00	29.72
1570	OG1	THR	719	14.908	37.198	23.251	1.00	33.15
1571	CG2	THR	719	12.906	38.435	23.520	1.00	32.70
1572	N	LYS	720	17.037	38.976	21.374	1.00	29.23
1573	CA	LYS	720	18.481	39.162	21.281	1.00	29.94
1574	C	LYS	720	18.709	40.525	20.625	1.00	25.15
1575	O	LYS	720	19.630	41.242	20.971	1.00	30.87

1576	CB	LYS	720	19.122	38.049	20.435	1.00	32.66
1577	CG	LYS	720	20.649	38.024	20.484	1.00	41.23
1578	CD	LYS	720	21.154	37.764	21.902	1.00	45.10
1579	CE	LYS	720	22.671	37.785	21.969	1.00	45.88
1580	NZ	LYS	720	23.231	37.484	23.350	1.00	50.22
1581	N	LEU	721	17.849	40.890	19.682	1.00	28.84
1582	CA	LEU	721	17.962	42.186	19.014	1.00	30.79
1583	C	LEU	721	17.799	43.313	20.049	1.00	31.46
1584	O	LEU	721	18.563	44.282	20.056	1.00	28.53
1585	CB	LEU	721	16.910	42.303	17.913	1.00	29.92
1586	CG	LEU	721	16.843	43.583	17.069	1.00	36.08
1587	CD1	LEU	721	16.109	43.302	15.767	1.00	37.87
1588	CD2	LEU	721	16.139	44.675	17.848	1.00	34.23
1589	N	LEU	722	16.813	43.179	20.930	1.00	26.83
1590	CA	LEU	722	16.603	44.188	21.966	1.00	32.06
1591	C	LEU	722	17.838	44.293	22.860	1.00	31.54
1592	O	LEU	722	18.268	45.405	23.208	1.00	27.43
1593	CB	LEU	722	15.368	43.847	22.804	1.00	28.40
1594	CG	LEU	722	14.020	43.968	22.085	1.00	33.60
1595	CD1	LEU	722	12.898	43.593	23.039	1.00	27.76
1596	CD2	LEU	722	13.817	45.402	21.578	1.00	36.94
1597	N	ASP	723	18.404	43.144	23.242	1.00	30.89
1598	CA	ASP	723	19.615	43.141	24.069	1.00	31.45
1599	C	ASP	723	20.725	43.895	23.355	1.00	33.06
1600	O	ASP	723	21.418	44.710	23.967	1.00	27.21
1601	CB	ASP	723	20.131	41.719	24.340	1.00	32.85
1602	CG	ASP	723	19.307	40.964	25.374	1.00	41.09
1603	OD1	ASP	723	18.366	41.546	25.954	1.00	34.77
1604	OD2	ASP	723	19.617	39.770	25.609	1.00	35.56
1605	N	SER	724	20.909	43.607	22.066	1.00	23.23
1606	CA	SER	724	21.960	44.274	21.307	1.00	29.88
1607	C	SER	724	21.770	45.780	21.172	1.00	27.44
1608	O	SER	724	22.735	46.513	20.960	1.00	28.18
1609	CB	SER	724	22.114	43.636	19.917	1.00	30.74
1610	OG	SER	724	20.999	43.898	19.058	1.00	99.90
1611	N	MET	725	20.537	46.251	21.314	1.00	27.04
1612	CA	MET	725	20.295	47.688	21.211	1.00	28.38
1613	C	MET	725	21.054	48.489	22.279	1.00	29.38
1614	O	MET	725	21.465	49.630	22.043	1.00	26.74
1615	CB	MET	725	18.795	47.975	21.288	1.00	27.75
1616	CG	MET	725	17.936	47.376	20.154	1.00	99.90
1617	SD	MET	725	16.267	48.046	20.234	1.00	99.90
1618	CE	MET	725	15.466	46.902	19.103	1.00	99.90
1619	N	HIS	726	21.256	47.893	23.446	1.00	25.82
1620	CA	HIS	726	21.974	48.580	24.517	1.00	26.55
1621	C	HIS	726	23.345	49.086	24.078	1.00	28.01
1622	O	HIS	726	23.671	50.249	24.293	1.00	26.18
1623	CB	HIS	726	22.127	47.669	25.745	1.00	27.98

1624	CG	HIS	726	20.895	47.574	26.592	1.00	31.07
1625	ND1	HIS	726	20.272	46.376	26.875	1.00	34.25
1626	CD2	HIS	726	20.192	48.527	27.252	1.00	25.45
1627	CE1	HIS	726	19.242	46.596	27.675	1.00	30.14
1628	NE2	HIS	726	19.172	47.892	27.917	1.00	32.22
1629	N	GLU	727	24.148	48.238	23.446	1.00	30.88
1630	CA	GLU	727	25.476	48.678	23.017	1.00	33.37
1631	C	GLU	727	25.357	49.683	21.881	1.00	32.18
1632	O	GLU	727	26.127	50.639	21.806	1.00	28.61
1633	CB	GLU	727	26.327	47.486	22.573	1.00	41.89
1634	CG	GLU	727	25.866	46.713	21.294	1.00	99.90
1635	CD	GLU	727	26.640	45.457	20.886	1.00	99.90
1636	OE1	GLU	727	26.334	44.770	19.921	1.00	99.90
1637	OE2	GLU	727	27.699	45.178	21.696	1.00	99.90
1638	N	VAL	728	24.394	49.464	20.991	1.00	25.95
1639	CA	VAL	728	24.183	50.377	19.877	1.00	24.45
1640	C	VAL	728	23.817	51.777	20.382	1.00	24.31
1641	O	VAL	728	24.412	52.774	19.976	1.00	24.16
1642	CB	VAL	728	23.092	49.899	18.861	1.00	25.35
1643	CG1	VAL	728	23.492	48.583	18.149	1.00	99.90
1644	CG2	VAL	728	22.782	50.963	17.778	1.00	99.90
1645	N	VAL	729	22.824	51.844	21.261	1.00	23.01
1646	CA	VAL	729	22.372	53.122	21.809	1.00	25.27
1647	C	VAL	729	23.466	53.875	22.575	1.00	22.87
1648	O	VAL	729	23.488	55.112	22.602	1.00	21.03
1649	CB	VAL	729	21.152	52.905	22.732	1.00	28.67
1650	CG1	VAL	729	20.798	54.197	23.450	1.00	30.03
1651	CG2	VAL	729	19.961	52.435	21.898	1.00	28.50
1652	N	GLU	730	24.366	53.132	23.200	1.00	23.37
1653	CA	GLU	730	25.459	53.754	23.940	1.00	23.75
1654	C	GLU	730	26.319	54.639	23.036	1.00	24.31
1655	O	GLU	730	26.805	55.687	23.470	1.00	23.94
1656	CB	GLU	730	26.325	52.689	24.594	1.00	23.23
1657	CG	GLU	730	27.399	53.266	25.500	1.00	34.73
1658	CD	GLU	730	28.403	52.304	26.141	1.00	99.90
1659	OE1	GLU	730	29.321	52.680	26.858	1.00	99.90
1660	OE2	GLU	730	28.179	50.996	25.838	1.00	99.90
1661	N	ASN	731	26.510	54.228	21.781	1.00	20.06
1662	CA	ASN	731	27.297	55.035	20.851	1.00	21.61
1663	C	ASN	731	26.511	56.290	20.509	1.00	20.55
1664	O	ASN	731	27.091	57.365	20.358	1.00	21.72
1665	CB	ASN	731	27.630	54.313	19.522	1.00	27.13
1666	CG	ASN	731	28.313	55.276	18.531	1.00	99.90
1667	OD1	ASN	731	27.690	55.787	17.614	1.00	99.90
1668	ND2	ASN	731	29.693	55.513	18.747	1.00	99.90
1669	N	LEU	732	25.195	56.156	20.355	1.00	18.60
1670	CA	LEU	732	24.372	57.322	20.073	1.00	19.89
1671	C	LEU	732	24.400	58.268	21.297	1.00	21.61

1672	O	LEU	732	24.496	59.486	21.145	1.00	18.84
1673	CB	LEU	732	22.936	56.899	19.764	1.00	24.80
1674	CG	LEU	732	22.703	55.942	18.590	1.00	32.83
1675	CD1	LEU	732	21.193	55.824	18.366	1.00	30.42
1676	CD2	LEU	732	23.369	56.464	17.329	1.00	34.48
1677	N	LEU	733	24.312	57.712	22.508	1.00	20.58
1678	CA	LEU	733	24.351	58.531	23.734	1.00	19.88
1679	C	LEU	733	25.661	59.317	23.841	1.00	23.80
1680	O	LEU	733	25.669	60.503	24.181	1.00	21.80
1681	CB	LEU	733	24.253	57.782	25.098	1.00	21.04
1682	CG	LEU	733	23.046	56.856	25.403	1.00	99.90
1683	CD1	LEU	733	22.981	56.535	26.912	1.00	99.90
1684	CD2	LEU	733	21.687	57.385	24.900	1.00	99.90
1685	N	ASN	734	26.774	58.653	23.543	1.00	22.67
1686	CA	ASN	734	28.066	59.318	23.616	1.00	21.83
1687	C	ASN	734	28.188	60.431	22.575	1.00	21.54
1688	O	ASN	734	28.645	61.526	22.886	1.00	20.75
1689	CB	ASN	734	29.250	58.341	23.367	1.00	20.66
1690	CG	ASN	734	29.379	57.211	24.413	1.00	99.90
1691	OD1	ASN	734	28.890	57.286	25.529	1.00	99.90
1692	ND2	ASN	734	30.142	56.095	23.981	1.00	99.90
1693	N	TYR	735	27.768	60.157	21.341	1.00	19.92
1694	CA	TYR	735	27.850	61.170	20.282	1.00	19.47
1695	C	TYR	735	26.977	62.389	20.650	1.00	22.05
1696	O	TYR	735	27.375	63.553	20.494	1.00	20.67
1697	CB	TYR	735	27.396	60.546	18.948	1.00	19.20
1698	CG	TYR	735	27.693	61.397	17.736	1.00	27.69
1699	CD1	TYR	735	26.945	62.546	17.461	1.00	26.53
1700	CD2	TYR	735	28.743	61.070	16.878	1.00	24.52
1701	CE1	TYR	735	27.237	63.347	16.359	1.00	30.01
1702	CE2	TYR	735	29.043	61.863	15.778	1.00	26.75
1703	CZ	TYR	735	28.285	62.998	15.525	1.00	33.34
1704	OH	TYR	735	28.416	63.738	14.398	1.00	39.29
1705	N	CYS	736	25.785	62.119	21.164	1.00	19.66
1706	CA	CYS	736	24.859	63.176	21.560	1.00	21.68
1707	C	CYS	736	25.421	64.067	22.674	1.00	20.24
1708	O	CYS	736	25.420	65.295	22.574	1.00	22.45
1709	CB	CYS	736	23.541	62.546	22.022	1.00	22.87
1710	SG	CYS	736	22.282	63.748	22.564	1.00	25.25
1711	N	PHE	737	25.901	63.448	23.738	1.00	21.55
1712	CA	PHE	737	26.445	64.208	24.862	1.00	24.47
1713	C	PHE	737	27.666	65.021	24.442	1.00	25.40
1714	O	PHE	737	27.856	66.143	24.922	1.00	28.02
1715	CB	PHE	737	26.898	63.269	26.010	1.00	24.44
1716	CG	PHE	737	27.315	64.017	27.260	1.00	99.90
1717	CD1	PHE	737	26.499	65.065	27.832	1.00	99.90
1718	CD2	PHE	737	28.542	63.654	27.928	1.00	99.90
1719	CE1	PHE	737	26.921	65.758	29.018	1.00	99.90

1720	CE2	PHE	737	28.954	64.332	29.127	1.00	99.90
1721	CZ	PHE	737	28.149	65.393	29.667	1.00	99.90
1722	N	GLN	738	28.497	64.463	23.562	1.00	23.21
1723	CA	GLN	738	29.658	65.202	23.063	1.00	23.92
1724	C	GLN	738	29.226	66.424	22.255	1.00	25.99
1725	O	GLN	738	29.753	67.514	22.440	1.00	27.51
1726	CB	GLN	738	30.559	64.293	22.179	1.00	27.01
1727	CG	GLN	738	31.843	64.932	21.588	1.00	99.90
1728	CD	GLN	738	31.591	65.903	20.416	1.00	99.90
1729	OE1	GLN	738	31.978	67.059	20.459	1.00	99.90
1730	NE2	GLN	738	30.947	65.358	19.278	1.00	99.90
1731	N	THR	739	28.287	66.230	21.337	1.00	25.80
1732	CA	THR	739	27.800	67.322	20.501	1.00	25.04
1733	C	THR	739	27.089	68.377	21.331	1.00	24.51
1734	O	THR	739	27.152	69.566	21.020	1.00	28.41
1735	CB	THR	739	26.837	66.791	19.405	1.00	22.97
1736	OG1	THR	739	27.460	65.817	18.573	1.00	23.34
1737	CG2	THR	739	26.356	67.912	18.511	1.00	25.92
1738	N	PHE	740	26.423	67.928	22.391	1.00	23.12
1739	CA	PHE	740	25.684	68.804	23.294	1.00	23.28
1740	C	PHE	740	26.683	69.700	24.034	1.00	26.81
1741	O	PHE	740	26.466	70.902	24.160	1.00	27.75
1742	CB	PHE	740	24.899	67.961	24.302	1.00	22.97
1743	CG	PHE	740	24.055	68.765	25.255	1.00	20.82
1744	CD1	PHE	740	22.905	69.411	24.823	1.00	21.56
1745	CD2	PHE	740	24.442	68.901	26.584	1.00	25.72
1746	CE1	PHE	740	22.143	70.187	25.698	1.00	26.99
1747	CE2	PHE	740	23.690	69.673	27.468	1.00	28.83
1748	CZ	PHE	740	22.537	70.318	27.025	1.00	24.76
1749	N	LEU	741	27.770	69.110	24.527	1.00	26.30
1750	CA	LEU	741	28.799	69.887	25.225	1.00	27.51
1751	C	LEU	741	29.519	70.858	24.274	1.00	30.83
1752	O	LEU	741	29.941	71.946	24.679	1.00	31.33
1753	CB	LEU	741	29.908	69.003	25.855	1.00	30.94
1754	CG	LEU	741	29.523	68.182	27.115	1.00	99.90
1755	CD1	LEU	741	30.665	67.202	27.464	1.00	99.90
1756	CD2	LEU	741	29.190	69.075	28.331	1.00	99.90
1757	N	ASP	742	29.648	70.476	23.005	1.00	29.65
1758	CA	ASP	742	30.336	71.327	22.034	1.00	30.69
1759	C	ASP	742	29.348	72.084	21.156	1.00	33.21
1760	O	ASP	742	29.743	72.682	20.152	1.00	36.42
1761	CB	ASP	742	31.235	70.464	21.144	1.00	34.22
1762	CG	ASP	742	32.171	71.209	20.181	1.00	99.90
1763	OD1	ASP	742	32.386	70.834	19.037	1.00	99.90
1764	OD2	ASP	742	32.709	72.339	20.732	1.00	99.90
1765	N	LYS	743	27.834	74.903	21.015	1.00	37.58
1766	CA	LYS	743	28.165	76.351	20.660	1.00	43.27
1767	C	LYS	743	29.304	76.341	19.648	1.00	46.14

1768	O	LYS	743	29.279	77.087	18.665	1.00	46.04
1769	CB	LYS	743	28.506	77.255	21.851	1.00	45.98
1770	CG	LYS	743	27.451	77.232	22.956	1.00	58.17
1771	CD	LYS	743	26.030	77.472	22.426	1.00	63.03
1772	CE	LYS	743	25.032	77.361	23.586	1.00	99.90
1773	NZ	LYS	743	23.692	77.759	23.119	1.00	99.90
1774	N	THR	744	30.284	75.470	19.863	1.00	43.89
1775	CA	THR	744	31.426	75.374	18.965	1.00	44.86
1776	C	THR	744	31.055	74.760	17.623	1.00	45.61
1777	O	THR	744	31.589	75.140	16.583	1.00	44.57
1778	CB	THR	744	32.532	74.549	19.617	1.00	49.14
1779	OG1	THR	744	32.980	75.173	20.814	1.00	99.90
1780	CG2	THR	744	33.816	74.345	18.784	1.00	99.90
1781	N	MET	745	30.135	73.805	17.654	1.00	44.06
1782	CA	MET	745	29.702	73.117	16.446	1.00	42.19
1783	C	MET	745	28.543	73.819	15.762	1.00	40.67
1784	O	MET	745	28.123	73.419	14.680	1.00	44.90
1785	CB	MET	745	29.360	71.629	16.758	1.00	39.53
1786	CG	MET	745	29.529	70.678	15.549	1.00	99.90
1787	SD	MET	745	29.499	68.900	15.994	1.00	99.90
1788	CE	MET	745	31.285	68.588	16.215	1.00	99.90
1789	N	SER	746	28.044	74.878	16.387	1.00	38.21
1790	CA	SER	746	26.919	75.618	15.851	1.00	35.93
1791	C	SER	746	25.688	74.721	15.769	1.00	34.57
1792	O	SER	746	24.879	74.855	14.856	1.00	33.32
1793	CB	SER	746	27.243	76.177	14.458	1.00	42.40
1794	OG	SER	746	28.273	77.165	14.476	1.00	50.36
1795	N	ILE	747	25.548	73.805	16.726	1.00	32.92
1796	CA	ILE	747	24.396	72.901	16.749	1.00	30.26
1797	C	ILE	747	23.448	73.310	17.879	1.00	31.81
1798	O	ILE	747	23.850	73.383	19.035	1.00	34.09
1799	CB	ILE	747	24.818	71.410	16.872	1.00	30.61
1800	CG2	ILE	747	23.605	70.496	17.156	1.00	99.90
1801	CG1	ILE	747	25.526	70.975	15.562	1.00	99.90
1802	CD1	ILE	747	26.220	69.611	15.607	1.00	99.90
1803	N	GLU	748	22.197	73.600	17.536	1.00	28.12
1804	CA	GLU	748	21.214	73.984	18.537	1.00	27.45
1805	C	GLU	748	20.405	72.802	19.068	1.00	27.94
1806	O	GLU	748	19.952	71.973	18.288	1.00	26.23
1807	CB	GLU	748	20.238	75.010	17.965	1.00	33.68
1808	CG	GLU	748	19.118	75.361	18.944	1.00	51.81
1809	CD	GLU	748	18.123	76.367	18.393	1.00	62.71
1810	OE1	GLU	748	18.298	76.824	17.240	1.00	63.38
1811	OE2	GLU	748	17.160	76.703	19.123	1.00	63.52
1812	N	PHE	749	20.236	72.733	20.392	1.00	25.35
1813	CA	PHE	749	19.440	71.681	21.029	1.00	24.39
1814	C	PHE	749	18.254	72.387	21.663	1.00	26.69
1815	O	PHE	749	18.441	73.352	22.404	1.00	27.33

1816	CB	PHE	749	20.204	70.946	22.155	1.00	25.14
1817	CG	PHE	749	21.267	69.994	21.674	1.00	21.63
1818	CD1	PHE	749	22.475	70.460	21.184	1.00	22.11
1819	CD2	PHE	749	21.036	68.626	21.691	1.00	23.38
1820	CE1	PHE	749	23.442	69.575	20.719	1.00	19.55
1821	CE2	PHE	749	21.992	67.725	21.228	1.00	24.14
1822	CZ	PHE	749	23.200	68.201	20.740	1.00	22.83
1823	N	PRO	750	17.022	71.932	21.382	1.00	23.73
1824	CA	PRO	750	15.833	72.563	21.961	1.00	22.74
1825	C	PRO	750	15.766	72.286	23.474	1.00	22.33
1826	O	PRO	750	16.501	71.459	24.004	1.00	22.26
1827	CB	PRO	750	14.683	71.901	21.198	1.00	24.51
1828	CG	PRO	750	15.346	71.451	19.899	1.00	30.94
1829	CD	PRO	750	16.607	70.851	20.478	1.00	29.32
1830	N	GLU	751	14.861	72.976	24.153	1.00	25.11
1831	CA	GLU	751	14.721	72.860	25.610	1.00	22.58
1832	C	GLU	751	14.366	71.515	26.232	1.00	21.81
1833	O	GLU	751	14.968	71.112	27.220	1.00	23.58
1834	CB	GLU	751	13.704	73.894	26.097	1.00	23.00
1835	CG	GLU	751	14.072	75.366	25.825	1.00	25.08
1836	CD	GLU	751	15.381	75.828	26.459	1.00	31.26
1837	OE1	GLU	751	15.751	75.341	27.550	1.00	31.56
1838	OE2	GLU	751	16.034	76.725	25.879	1.00	31.17
1839	N	MET	752	13.369	70.820	25.692	1.00	20.50
1840	CA	MET	752	12.989	69.543	26.286	1.00	22.40
1841	C	MET	752	14.077	68.499	26.093	1.00	20.88
1842	O	MET	752	14.348	67.698	26.987	1.00	22.84
1843	CB	MET	752	11.659	69.064	25.692	1.00	28.13
1844	CG	MET	752	10.536	70.073	25.898	1.00	30.10
1845	SD	MET	752	8.936	69.576	25.227	1.00	36.75
1846	CE	MET	752	9.384	69.107	23.548	1.00	29.48
1847	N	LEU	753	14.719	68.514	24.932	1.00	22.18
1848	CA	LEU	753	15.778	67.555	24.665	1.00	20.40
1849	C	LEU	753	16.986	67.882	25.514	1.00	20.24
1850	O	LEU	753	17.662	66.988	26.013	1.00	20.23
1851	CB	LEU	753	16.131	67.658	23.154	1.00	24.51
1852	CG	LEU	753	17.165	66.660	22.591	1.00	99.90
1853	CD1	LEU	753	16.675	65.204	22.693	1.00	99.90
1854	CD2	LEU	753	17.507	66.994	21.122	1.00	99.90
1855	N	ALA	754	17.262	69.171	25.680	1.00	22.17
1856	CA	ALA	754	18.392	69.574	26.501	1.00	24.13
1857	C	ALA	754	18.157	69.098	27.942	1.00	24.76
1858	O	ALA	754	19.097	68.690	28.634	1.00	20.25
1859	CB	ALA	754	18.553	71.102	26.477	1.00	24.96
1860	N	GLU	755	16.907	69.162	28.393	1.00	21.90
1861	CA	GLU	755	16.600	68.727	29.754	1.00	25.07
1862	C	GLU	755	16.830	67.238	29.977	1.00	25.56
1863	O	GLU	755	17.432	66.860	30.971	1.00	26.95

1864	CB	GLU	755	15.163	69.086	30.153	1.00	26.93
1865	CG	GLU	755	14.785	68.556	31.538	1.00	30.33
1866	CD	GLU	755	15.673	69.098	32.663	1.00	45.68
1867	OE1	GLU	755	16.238	70.205	32.515	1.00	48.37
1868	OE2	GLU	755	15.790	68.424	33.714	1.00	40.75
1869	N	ILE	756	16.358	66.385	29.072	1.00	23.66
1870	CA	ILE	756	16.559	64.963	29.273	1.00	24.09
1871	C	ILE	756	18.031	64.596	29.179	1.00	22.11
1872	O	ILE	756	18.500	63.731	29.918	1.00	23.47
1873	CB	ILE	756	15.714	64.091	28.272	1.00	25.40
1874	CG2	ILE	756	15.854	62.560	28.536	1.00	99.90
1875	CG1	ILE	756	14.191	64.439	28.230	1.00	99.90
1876	CD1	ILE	756	13.396	63.843	27.050	1.00	99.90
1877	N	ILE	757	18.775	65.274	28.301	1.00	20.76
1878	CA	ILE	757	20.201	64.977	28.158	1.00	20.13
1879	C	ILE	757	20.932	65.313	29.441	1.00	23.37
1880	O	ILE	757	21.695	64.500	29.980	1.00	25.36
1881	CB	ILE	757	20.826	65.763	26.979	1.00	19.24
1882	CG1	ILE	757	20.290	65.215	25.661	1.00	22.39
1883	CG2	ILE	757	22.352	65.650	27.013	1.00	18.20
1884	CD1	ILE	757	20.522	66.153	24.469	1.00	26.26
1885	N	THR	758	20.684	66.509	29.948	1.00	23.60
1886	CA	THR	758	21.324	66.958	31.177	1.00	30.05
1887	C	THR	758	20.880	66.163	32.401	1.00	27.97
1888	O	THR	758	21.666	65.921	33.317	1.00	31.89
1889	CB	THR	758	21.042	68.460	31.398	1.00	24.81
1890	OG1	THR	758	21.578	69.230	30.329	1.00	99.90
1891	CG2	THR	758	21.647	69.091	32.671	1.00	99.90
1892	N	ASN	759	19.624	65.745	32.427	1.00	28.98
1893	CA	ASN	759	19.128	65.006	33.580	1.00	30.10
1894	C	ASN	759	19.657	63.578	33.713	1.00	29.70
1895	O	ASN	759	19.837	63.092	34.828	1.00	30.09
1896	CB	ASN	759	17.596	64.990	33.572	1.00	29.66
1897	CG	ASN	759	16.888	66.349	33.553	1.00	99.90
1898	OD1	ASN	759	16.425	66.829	32.529	1.00	99.90
1899	ND2	ASN	759	16.796	67.026	34.666	1.00	99.90
1900	N	GLN	760	19.935	62.906	32.599	1.00	26.34
1901	CA	GLN	760	20.377	61.526	32.700	1.00	23.29
1902	C	GLN	760	21.537	61.004	31.859	1.00	23.47
1903	O	GLN	760	22.127	59.991	32.231	1.00	24.44
1904	CB	GLN	760	19.199	60.581	32.419	1.00	29.83
1905	CG	GLN	760	17.964	60.724	33.272	1.00	31.14
1906	CD	GLN	760	18.228	60.589	34.752	1.00	37.37
1907	OE1	GLN	760	19.070	59.800	35.180	1.00	33.07
1908	NE2	GLN	760	17.354	61.340	35.577	1.00	42.40
1909	N	ILE	761	21.852	61.619	30.719	1.00	24.92
1910	CA	ILE	761	22.919	61.043	29.888	1.00	27.91
1911	C	ILE	761	24.248	60.745	30.555	1.00	27.51

1912	O	ILE	761	24.799	59.664	30.369	1.00	30.01
1913	CB	ILE	761	23.140	61.825	28.556	1.00	28.45
1914	CG2	ILE	761	24.335	61.277	27.746	1.00	99.90
1915	CG1	ILE	761	21.864	61.785	27.655	1.00	99.90
1916	CD1	ILE	761	21.527	60.456	26.954	1.00	99.90
1917	N	PRO	762	24.805	61.698	31.308	1.00	27.54
1918	CA	PRO	762	26.081	61.376	31.948	1.00	27.73
1919	C	PRO	762	25.963	60.143	32.868	1.00	24.86
1920	O	PRO	762	26.847	59.293	32.895	1.00	25.75
1921	CB	PRO	762	26.399	62.656	32.715	1.00	27.68
1922	CG	PRO	762	25.760	63.728	31.833	1.00	26.00
1923	CD	PRO	762	24.403	63.078	31.631	1.00	28.16
1924	N	LYS	763	24.872	60.049	33.620	1.00	23.19
1925	CA	LYS	763	24.668	58.912	34.523	1.00	24.99
1926	C	LYS	763	24.555	57.617	33.722	1.00	26.95
1927	O	LYS	763	25.189	56.609	34.046	1.00	26.77
1928	CB	LYS	763	23.391	59.124	35.346	1.00	31.71
1929	CG	LYS	763	23.098	58.039	36.368	1.00	36.39
1930	CD	LYS	763	21.730	58.277	37.013	1.00	41.59
1931	CE	LYS	763	21.668	59.627	37.724	1.00	46.46
1932	NZ	LYS	763	20.287	59.994	38.237	1.00	52.55
1933	N	TYR	764	23.747	57.644	32.667	1.00	25.62
1934	CA	TYR	764	23.577	56.459	31.820	1.00	25.44
1935	C	TYR	764	24.904	56.027	31.211	1.00	28.84
1936	O	TYR	764	25.260	54.850	31.252	1.00	23.14
1937	CB	TYR	764	22.588	56.747	30.692	1.00	25.43
1938	CG	TYR	764	21.157	57.110	31.106	1.00	99.90
1939	CD1	TYR	764	20.748	58.447	31.092	1.00	99.90
1940	CD2	TYR	764	20.258	56.118	31.507	1.00	99.90
1941	CE1	TYR	764	19.456	58.789	31.480	1.00	99.90
1942	CE2	TYR	764	18.965	56.463	31.896	1.00	99.90
1943	CZ	TYR	764	18.566	57.796	31.882	1.00	99.90
1944	OH	TYR	764	17.298	58.130	32.266	1.00	99.90
1945	N	SER	765	25.633	56.971	30.624	1.00	26.45
1946	CA	SER	765	26.936	56.647	30.027	1.00	29.61
1947	C	SER	765	27.932	56.082	31.028	1.00	30.39
1948	O	SER	765	28.733	55.198	30.698	1.00	32.46
1949	CB	SER	765	27.545	57.887	29.360	1.00	27.19
1950	OG	SER	765	27.957	58.882	30.304	1.00	99.90
1951	N	ASN	766	27.897	56.594	32.249	1.00	28.14
1952	CA	ASN	766	28.813	56.116	33.266	1.00	29.10
1953	C	ASN	766	28.409	54.720	33.734	1.00	29.03
1954	O	ASN	766	29.116	54.104	34.515	1.00	32.66
1955	CB	ASN	766	28.845	57.089	34.433	1.00	25.78
1956	CG	ASN	766	29.221	58.540	34.116	1.00	99.90
1957	OD1	ASN	766	28.382	59.422	34.006	1.00	99.90
1958	ND2	ASN	766	30.480	58.839	33.935	1.00	99.90
1959	N	GLY	767	27.274	54.218	33.247	1.00	30.49

1960	CA	GLY	767	26.826	52.893	33.652	1.00	30.14
1961	C	GLY	767	26.212	52.842	35.048	1.00	28.27
1962	O	GLY	767	26.277	51.815	35.724	1.00	35.23
1963	N	ASN	768	25.613	53.942	35.492	1.00	27.77
1964	CA	ASN	768	25.005	53.977	36.817	1.00	31.40
1965	C	ASN	768	23.506	53.689	36.729	1.00	28.03
1966	O	ASN	768	22.691	54.330	37.391	1.00	31.74
1967	CB	ASN	768	25.266	55.335	37.472	1.00	32.66
1968	CG	ASN	768	26.730	55.763	37.620	1.00	99.90
1969	OD1	ASN	768	27.260	56.553	36.853	1.00	99.90
1970	ND2	ASN	768	27.441	55.248	38.587	1.00	99.90
1971	N	ILE	769	23.172	52.725	35.879	1.00	29.55
1972	CA	ILE	769	21.802	52.273	35.653	1.00	28.30
1973	C	ILE	769	21.875	50.778	35.406	1.00	31.38
1974	O	ILE	769	22.944	50.244	35.111	1.00	28.00
1975	CB	ILE	769	21.151	52.942	34.422	1.00	27.98
1976	CG2	ILE	769	19.658	52.531	34.229	1.00	99.90
1977	CG1	ILE	769	21.229	54.503	34.411	1.00	99.90
1978	CD1	ILE	769	20.887	55.185	33.070	1.00	99.90
1979	N	LYS	770	20.731	50.112	35.511	1.00	28.65
1980	CA	LYS	770	20.657	48.673	35.344	1.00	27.13
1981	C	LYS	770	19.961	48.263	34.051	1.00	27.33
1982	O	LYS	770	18.737	48.229	33.971	1.00	26.71
1983	CB	LYS	770	19.922	48.079	36.543	1.00	30.31
1984	CG	LYS	770	19.641	46.598	36.440	1.00	36.48
1985	CD	LYS	770	18.845	46.130	37.649	1.00	42.65
1986	CE	LYS	770	18.386	44.692	37.468	1.00	45.66
1987	NZ	LYS	770	19.510	43.707	37.195	1.00	41.46
1988	N	LYS	771	20.743	47.945	33.013	1.00	29.35
1989	CA	LYS	771	20.153	47.543	31.738	1.00	29.76
1990	C	LYS	771	19.501	46.177	31.940	1.00	32.65
1991	O	LYS	771	20.108	45.300	32.554	1.00	31.57
1992	CB	LYS	771	21.372	47.462	30.817	1.00	32.15
1993	CG	LYS	771	21.013	47.119	29.349	1.00	99.90
1994	CD	LYS	771	22.214	46.965	28.412	1.00	99.90
1995	CE	LYS	771	21.719	46.557	27.018	1.00	99.90
1996	NZ	LYS	771	22.849	46.576	26.072	1.00	99.90
1997	N	LEU	772	18.269	45.986	31.471	1.00	26.08
1998	CA	LEU	772	17.643	44.678	31.634	1.00	28.80
1999	C	LEU	772	17.957	43.890	30.386	1.00	32.70
2000	O	LEU	772	17.814	44.396	29.272	1.00	32.54
2001	CB	LEU	772	16.125	44.804	31.825	1.00	28.21
2002	CG	LEU	772	15.741	45.638	33.053	1.00	27.44
2003	CD1	LEU	772	14.223	45.661	33.216	1.00	25.95
2004	CD2	LEU	772	16.400	45.046	34.305	1.00	28.60
2005	N	LEU	773	18.403	42.656	30.572	1.00	29.11
2006	CA	LEU	773	18.768	41.800	29.447	1.00	32.04
2007	C	LEU	773	17.933	40.528	29.413	1.00	33.98

2008	O	LEU	773	17.604	39.979	30.462	1.00	35.14
2009	CB	LEU	773	20.253	41.426	29.552	1.00	30.80
2010	CG	LEU	773	21.245	42.595	29.527	1.00	41.73
2011	CD1	LEU	773	22.654	42.099	29.847	1.00	37.07
2012	CD2	LEU	773	21.198	43.263	28.165	1.00	38.20
2013	N	PHE	774	17.580	40.075	28.211	1.00	30.93
2014	CA	PHE	774	16.815	38.838	28.065	1.00	36.94
2015	C	PHE	774	17.728	37.626	28.056	1.00	37.82
2016	O	PHE	774	17.306	36.518	28.390	1.00	40.73
2017	CB	PHE	774	16.011	38.820	26.771	1.00	33.98
2018	CG	PHE	774	14.787	39.666	26.818	1.00	31.86
2019	CD1	PHE	774	13.620	39.164	27.384	1.00	27.98
2020	CD2	PHE	774	14.803	40.967	26.346	1.00	29.84
2021	CE1	PHE	774	12.488	39.955	27.478	1.00	34.01
2022	CE2	PHE	774	13.668	41.769	26.435	1.00	31.12
2023	CZ	PHE	774	12.514	41.264	27.002	1.00	31.58
2024	N	HIS	775	18.975	37.839	27.659	1.00	39.64
2025	CA	HIS	775	19.937	36.755	27.605	1.00	43.59
2026	C	HIS	775	21.178	37.074	28.410	1.00	45.74
2027	O	HIS	775	21.780	38.133	28.258	1.00	48.72
2028	CB	HIS	775	20.286	36.470	26.149	1.00	41.38
2029	CG	HIS	775	19.079	36.205	25.308	1.00	44.29
2030	ND1	HIS	775	18.211	35.169	25.572	1.00	49.69
2031	CD2	HIS	775	18.541	36.892	24.274	1.00	48.24
2032	CE1	HIS	775	17.187	35.231	24.738	1.00	50.45
2033	NE2	HIS	775	17.364	36.268	23.940	1.00	49.57
2034	N	GLN	776	21.531	36.142	29.288	1.00	50.39
2035	CA	GLN	776	22.698	36.254	30.150	1.00	56.63
2036	C	GLN	776	23.960	36.339	29.302	1.00	53.01
2037	O	GLN	776	23.958	35.647	28.265	1.00	56.94
2038	CB	GLN	776	22.748	35.026	31.061	1.00	57.98
2039	CG	GLN	776	22.461	33.738	30.299	1.00	61.12
2040	CD	GLN	776	22.409	32.412	31.067	1.00	99.90
2041	OE1	GLN	776	22.143	31.364	30.499	1.00	99.90
2042	NE2	GLN	776	22.627	32.394	32.357	1.00	99.90
2043	CB	GLU	685	16.805	65.125	37.380	1.00	63.65
2044	CG	GLU	685	16.240	65.106	38.791	1.00	63.87
2045	CD	GLU	685	15.337	63.914	39.036	1.00	64.23
2046	OE1	GLU	685	14.222	63.893	38.474	1.00	64.28
2047	OE2	GLU	685	15.741	62.998	39.783	1.00	64.53
2048	C	GLU	685	16.202	67.392	36.510	1.00	61.94
2049	O	GLU	685	16.230	67.976	35.426	1.00	62.27
2050	N	GLU	685	18.175	67.207	37.988	1.00	62.90
2051	CA	GLU	685	17.353	66.483	36.931	1.00	62.73
2052	N	ARG	686	15.189	67.501	37.368	1.00	60.58
2053	CA	ARG	686	14.026	68.343	37.098	1.00	59.13
2054	CB	ARG	686	14.484	69.737	36.657	1.00	60.07
2055	CG	ARG	686	13.371	70.752	36.441	1.00	61.27

2056	CD	ARG	686	12.980	71.452	37.735	1.00	62.16
2057	NE	ARG	686	12.286	72.710	37.474	1.00	63.43
2058	CZ	ARG	686	11.075	72.803	36.934	1.00	64.44
2059	NH1	ARG	686	10.244	71.724	36.777	1.00	64.89
2060	NH2	ARG	686	10.622	74.033	36.555	1.00	65.34
2061	C	ARG	686	13.106	67.744	36.030	1.00	57.39
2062	O	ARG	686	12.108	67.097	36.352	1.00	58.48
2063	N	HIS	687	13.452	67.962	34.764	1.00	54.71
2064	CA	HIS	687	12.666	67.470	33.632	1.00	51.16
2065	CB	HIS	687	12.415	65.962	33.752	1.00	51.72
2066	CG	HIS	687	13.660	65.132	33.685	1.00	51.47
2067	CD2	HIS	687	14.122	64.297	32.725	1.00	51.61
2068	ND1	HIS	687	14.601	65.118	34.691	1.00	52.04
2069	CE1	HIS	687	15.590	64.308	34.354	1.00	51.83
2070	NE2	HIS	687	15.324	63.798	33.166	1.00	51.34
2071	C	HIS	687	11.333	68.204	33.547	1.00	48.80
2072	O	HIS	687	10.272	67.584	33.498	1.00	48.44
2073	N	ALA	688	11.400	69.531	33.519	1.00	45.79
2074	CA	ALA	688	10.208	70.370	33.454	1.00	43.75
2075	CB	ALA	688	10.613	71.841	33.459	1.00	43.70
2076	C	ALA	688	9.318	70.085	32.246	1.00	41.94
2077	O	ALA	688	8.143	69.755	32.400	1.00	40.94
2078	N	ILE	689	9.879	70.215	31.048	1.00	40.75
2079	CA	ILE	689	9.121	69.990	29.823	1.00	39.42
2080	CB	ILE	689	10.010	70.192	28.579	1.00	39.12
2081	CG2	ILE	689	9.240	69.818	27.316	1.00	38.63
2082	CG1	ILE	689	10.466	71.652	28.513	1.00	38.90
2083	CD1	ILE	689	11.342	71.978	27.322	1.00	39.20
2084	C	ILE	689	8.483	68.606	29.772	1.00	38.83
2085	O	ILE	689	7.292	68.474	29.487	1.00	37.60
2086	N	LEU	690	9.276	67.579	30.053	1.00	38.40
2087	CA	LEU	690	8.774	66.213	30.040	1.00	38.63
2088	CB	LEU	690	9.893	65.247	30.435	1.00	39.36
2089	CG	LEU	690	9.858	63.847	29.820	1.00	40.30
2090	CD1	LEU	690	11.172	63.130	30.105	1.00	39.81
2091	CD2	LEU	690	8.682	63.064	30.374	1.00	41.50
2092	C	LEU	690	7.602	66.111	31.017	1.00	39.78
2093	O	LEU	690	6.543	65.578	30.679	1.00	38.83
2094	N	HIS	691	7.789	66.633	32.227	1.00	40.27
2095	CA	HIS	691	6.726	66.614	33.229	1.00	41.72
2096	CB	HIS	691	7.181	67.316	34.509	1.00	43.49
2097	CG	HIS	691	7.873	66.413	35.480	1.00	45.34
2098	CD2	HIS	691	9.155	66.387	35.917	1.00	46.24
2099	ND1	HIS	691	7.226	65.386	36.131	1.00	46.60
2100	CE1	HIS	691	8.079	64.767	36.928	1.00	46.83
2101	NE2	HIS	691	9.256	65.355	36.817	1.00	47.22
2102	C	HIS	691	5.487	67.312	32.681	1.00	41.36
2103	O	HIS	691	4.372	66.800	32.795	1.00	41.77

2104	N	ARG	692	5.692	68.482	32.085	1.00	40.51
2105	CA	ARG	692	4.592	69.250	31.511	1.00	40.58
2106	CB	ARG	692	5.131	70.500	30.815	1.00	41.97
2107	CG	ARG	692	4.061	71.442	30.275	1.00	44.31
2108	CD	ARG	692	4.690	72.501	29.383	1.00	46.39
2109	NE	ARG	692	5.286	71.900	28.191	1.00	48.87
2110	CZ	ARG	692	6.094	72.537	27.349	1.00	49.52
2111	NH1	ARG	692	6.586	73.791	27.593	1.00	50.67
2112	NH2	ARG	692	6.422	71.914	26.185	1.00	49.63
2113	C	ARG	692	3.823	68.392	30.508	1.00	39.77
2114	O	ARG	692	2.612	68.204	30.642	1.00	38.70
2115	N	LEU	693	4.532	67.870	29.509	1.00	38.99
2116	CA	LEU	693	3.917	67.031	28.482	1.00	39.44
2117	CB	LEU	693	4.984	66.418	27.567	1.00	38.36
2118	CG	LEU	693	5.747	67.337	26.608	1.00	38.71
2119	CD1	LEU	693	6.769	66.517	25.841	1.00	37.17
2120	CD2	LEU	693	4.781	68.014	25.646	1.00	37.74
2121	C	LEU	693	3.082	65.913	29.088	1.00	40.12
2122	O	LEU	693	1.998	65.599	28.598	1.00	40.20
2123	N	LEU	694	3.591	65.310	30.155	1.00	41.30
2124	CA	LEU	694	2.880	64.224	30.814	1.00	43.03
2125	CB	LEU	694	3.814	63.511	31.793	1.00	41.27
2126	CG	LEU	694	4.944	62.707	31.142	1.00	40.09
2127	CD1	LEU	694	5.933	62.249	32.194	1.00	39.04
2128	CD2	LEU	694	4.351	61.515	30.400	1.00	39.24
2129	C	LEU	694	1.634	64.710	31.547	1.00	45.64
2130	O	LEU	694	0.736	63.920	31.838	1.00	44.78
2131	N	GLN	695	1.575	66.007	31.832	1.00	49.29
2132	CA	GLN	695	0.436	66.580	32.546	1.00	53.51
2133	CB	GLN	695	0.780	67.978	33.075	1.00	53.94
2134	CG	GLN	695	2.068	68.066	33.890	1.00	54.96
2135	CD	GLN	695	2.065	67.191	35.133	1.00	55.61
2136	OE1	GLN	695	3.023	67.202	35.911	1.00	55.52
2137	NE2	GLN	695	0.874	66.592	35.592	1.00	55.62
2138	C	GLN	695	-0.834	66.666	31.699	1.00	55.94
2139	O	GLN	695	-1.931	66.813	32.236	1.00	55.76
2140	N	GLU	696	-0.686	66.579	30.380	1.00	58.97
2141	CA	GLU	696	-1.829	66.652	29.470	1.00	62.61
2142	CB	GLU	696	-2.620	67.945	29.711	1.00	63.02
2143	CG	GLU	696	-1.785	69.190	30.082	1.00	63.82
2144	CD	GLU	696	-0.758	69.598	29.037	1.00	64.13
2145	OE1	GLU	696	-1.131	69.774	27.856	1.00	64.51
2146	OE2	GLU	696	0.422	69.758	29.402	1.00	64.16
2147	C	GLU	696	-1.374	66.630	28.019	1.00	64.98
2148	O	GLU	696	-2.107	66.233	27.112	1.00	65.58
2149	N	GLY	697	-0.140	67.073	27.836	1.00	67.35
2150	CA	GLY	697	0.479	67.171	26.535	1.00	70.03
2151	C	GLY	697	1.252	68.446	26.701	1.00	71.80

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2152	O	GLY	697	1.323	69.262	25.756	1.00	71.76
2153	OXT	GLY	697	1.783	68.647	27.817	1.00	71.76

It will be understood that various details of the invention may be changed without departing from the scope of the invention. Furthermore, the foregoing description is for the purpose of illustration only, and not for the purpose of
5 limitation—the invention being defined by the claims.

CLAIMS

What is claimed is:

1. A method of modifying a test NR polypeptide, the method comprising:
 - 5 (a) providing a test NR polypeptide sequence having a characteristic that is targeted for modification;
 - (b) aligning the test NR polypeptide sequence with at least one reference NR polypeptide sequence for which an X-ray structure is available, wherein the at least one reference NR polypeptide
10 sequence has a characteristic that is desired for the test NR polypeptide;
 - (c) building a three-dimensional model for the test NR polypeptide using the three-dimensional coordinates of the X-ray structure(s) of the at least one reference polypeptide and its sequence alignment with the
15 test NR polypeptide sequence;
 - (d) examining the three-dimensional model of the test NR polypeptide for a difference in an amino acid residue as compared to the at least one reference polypeptide, wherein the residues are associated with the desired characteristic; and
20 (e) mutating an amino acid residue in the test NR polypeptide sequence located at a difference identified in step (d) to a residue associated with the desired characteristic, whereby the test NR polypeptide is modified.
- 25 2. The method of claim 1, wherein the reference NR polypeptide sequence is a PR sequence, and wherein the test polypeptide sequence is a GR polypeptide sequence.
- 30 3. The method of claim 1, wherein the polypeptide of a crystalline GR LBD is used as the reference polypeptide sequence.
4. The method of claim 1, wherein the method is carried out in a bacterial expression system.

5. The method of claim 1, wherein the bacteria is *E. coli*.

6. A method for modifying a test NR polypeptide to improve the solubility, stability in solution and other solution behavior, to alter and preferably improve the folding and stability of the folded structure, to alter and preferably improve the ability to form ordered crystals, or combination thereof, the method comprising:

- 10 (a) providing a test NR polypeptide sequence for which the solubility, stability in solution, other solution behavior, tendency to fold properly, ability to form ordered crystals, or combination thereof is different from that desired;
- 15 (b) aligning the test NR polypeptide sequence with the sequences of one or more reference NR polypeptides for which the X-ray structure is available and for which the solution properties, folding behavior and crystallization properties are closer to those desired;
- (c) building a three-dimensional model for the test NR polypeptide using the three-dimensional coordinates of the X-ray structure(s) of the one or more of reference polypeptides and their sequence alignment with the test NR polypeptide sequence;
- 20 (d) examining the three-dimensional model of the test NR polypeptide for lipophilic side-chains that are exposed to solvent, for clusters of two or more lipophilic side-chains exposed to solvent, for lipophilic pockets and clefts on the surface of the protein model, for sites on the surface of the protein model that are more lipophilic than the corresponding sites on the structure(s) of the reference NR polypeptide(s), or combinations thereof;
- 25 (e) for each residue identified in step (d), mutating the amino acid to an amino acid with different hydrophilicity, whereby the exposed lipophilic sites are reduced, and the solution properties improved;
- 30 (f) examining the three-dimensional model at each site where the amino acid in the test NR polypeptide is different from the amino acid at the corresponding position in the reference NR polypeptide,

and checking whether the amino acid in the test NR polypeptide makes favorable interactions with the atoms that lie around it in the three-dimensional model, considering the side-chain conformations predicted in step (c), considering alternative conformations of the side-chains, considering the presence of water molecules, or combinations thereof;

(g) for each residue identified in step (f) as not making favorable interactions with the atoms that lie around it, mutating the residue to another amino acid that makes favorable interactions with the atoms that lie around it, thereby promoting the tendency for the test NR polypeptide to fold into a stable structure with improved solution properties, less tendency to unfold, and greater tendency to form ordered crystals;

(h) examining the three-dimensional model at each residue position where the amino acid in the test NR polypeptide is different from the amino acid at the corresponding position in the reference NR polypeptide, and checking whether the steric packing, hydrogen bonding and other energetic interactions could be improved by mutating that residue or any one or more of the surrounding residues lying within 8 angstroms in the three-dimensional model;

(i) for each residue position identified in step (h) as potentially allowing an improvement in the packing, hydrogen bonding and energetic interactions, mutating those residues individually or in combination to residues that improve the packing, hydrogen bonding, energetic interactions, and combinations thereof, thereby promoting the tendency for the test NR polypeptide to fold into a stable structure with improved solution properties, less tendency to unfold, and greater tendency to form ordered crystals.

7. The method of claim 6, further comprising optimizing the side-chain conformations in the three-dimensional model of the test NR polypeptide by generating many alternative side-chain conformations, refining by energy minimization, and selecting side-chain conformations with lower energy.

8. The method of claim 6, wherein the mutating of step (e) further comprises a mutation to a more hydrophilic amino acid.

5 9. The method of claim 6, wherein the reference NR polypeptide is PR, and wherein the test NR polypeptide is GR α .

10 10. The method of claim 6, wherein the reference NR polypeptide is GR α , and wherein the test NR polypeptide is GR β or MR.

11. The method of claim 6, wherein the method is carried out in a bacterial expression system.

15 12. The method of claim 6, wherein the bacteria is *E. coli*.

13. An isolated GR polypeptide comprising a mutation in a ligand binding domain, wherein the mutation alters the solubility of the ligand binding domain.

20

14. An isolated GR polypeptide, or functional portion thereof, having one or more mutations comprising a substitution of a hydrophobic amino acid residue by a hydrophilic amino acid residue in a ligand binding domain.

25 15. The isolated polypeptide of claims 13 or 14, wherein the mutation is at a residue selected from the group consisting of V552, W557, F602, L636, Y648, W712, L741, L535, V538, C638, M691, V702, Y648, Y660, L685, M691, V702, W712, L733, Y764 and combinations thereof.

30 16. The isolated polypeptide of claims 13 or 14, wherein the mutation is selected from the group consisting of V552K, W557S, F602S, F602D, F602E, F602Y, F602T, F602N, F602C, L636E, Y648Q, W712S, L741R, L535T, V538S, C638S, M691T, V702T, W712T and combinations thereof.

17. An isolated GR LBD polypeptide, or functional portion thereof, having a F602S mutation or a F602D mutation, or a phenylalanine to serine or phenylalanine to aspartic acid mutation at an analogous position in the sequence
5 in any polypeptide based on sequence alignment to GR α .

18. The isolated polypeptide of claim 17, wherein the polypeptide has the sequence of SEQ ID NO:12 or 14.

10

19. An isolated nucleic acid molecule encoding a GR polypeptide of any of claims 13-18.

20. A chimeric gene, comprising the nucleic acid molecule of claim 19
15 operably linked to a heterologous promoter.

21. A vector comprising the chimeric gene of claim 20.

22. A host cell comprising the chimeric gene of claim 20.

20

23. A method of detecting a nucleic acid molecule that encodes a GR polypeptide, the method comprising:

- (a) procuring a biological sample comprising nucleic acid material;
- (b) hybridizing the nucleic acid molecule of claim 19 under stringent hybridization conditions to the biological sample of (a), thereby forming a duplex structure between the nucleic acid of claim 19 and a nucleic acid within the biological sample; and
- (c) detecting the duplex structure of (b), whereby a GR encoding nucleic acid molecule is detected.

25

30

24. An antibody that specifically recognizes a GR polypeptide of any of claims 13-18.

25. A method for producing an antibody that specifically recognizes a GR polypeptide, the method comprising:

- (a) recombinantly or synthetically producing a GR polypeptide of any of claims 13-18, or portion thereof;
- (b) formulating the polypeptide of (a) whereby it is an effective immunogen;
- 10 (c) administering to an animal the formulation of (b) to generate an immune response in the animal comprising production of antibodies, wherein antibodies are present in the blood serum of the animal; and
- (d) collecting the blood serum from the animal of (c), the blood serum comprising antibodies that specifically recognize a GR polypeptide.

15

26. A method for detecting a level of GR polypeptide, the method comprising:

- (a) obtaining a biological sample comprising peptidic material; and
- 20 (b) detecting a GR polypeptide in the biological sample of (a) by immunochemical reaction with the antibody of claim 24, whereby an amount of GR polypeptide in a sample is determined.

20

27. A method for identifying a substance that modulates GR LBD function, the method comprising:

- 25 (a) isolating a GR LBD polypeptide of any of claims 13-18;
- (b) exposing the isolated GR polypeptide to a plurality of substances;
- (c) assaying binding of a substance to the isolated GR polypeptide; and

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- (d) selecting a substance that demonstrates specific binding to the isolated GR LBD polypeptide.

28. A substantially pure GR ligand binding domain polypeptide in
5 crystalline form.

29. The polypeptide of claim 28, wherein the crystalline form comprises
lattice constants of $a = b = 126.014 \text{ \AA}$, $c = 86.312 \text{ \AA}$, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 120^\circ$.

10 30. The polypeptide of claim 28 or 29, wherein the crystalline form is a
hexagonal crystalline form.

31. The polypeptide of claim 28 or 29, wherein the crystalline form has a
space group of $P6_1$.

15 32. The polypeptide of claim 28 or 29, wherein the GR α ligand binding
domain polypeptide has the amino acid sequence shown in any one of SEQ ID
NOs: 12, 14, 16 and 31.

20 33. The polypeptide of claim 28 or 29, wherein the GR ligand binding
domain polypeptide is in complex with a ligand.

34. The polypeptide of claim 33, wherein the ligand is a steroid.

25 35. The polypeptide of claim 34, wherein the steroid is dexamethasone.

36. The polypeptide of claim 28 or 29, wherein the GR ligand binding
domain polypeptide is in complex with a ligand and a peptide.

30 37. The polypeptide of claim 36, wherein the ligand is a steroid.

38. The polypeptide of claim 37, wherein the steroid is dexamethasone.

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39. The polypeptide of claim 38, wherein the ligand is a steroid and the peptide is a fragment of a co-activator.

5 40. The polypeptide of claim 36, wherein the ligand is a steroid and the peptide is a fragment of a co-repressor.

41. The polypeptide of claim 36, wherein the ligand is dexamethasone and the peptide comprises an LXXLL (SEQ ID NO:18) motif.
10

42. The polypeptide of claim 36, wherein the peptide is a fragment of a TIF2 protein.

43. The polypeptide of claim 42, wherein the ligand is dexamethasone and the peptide has the amino acid sequence shown in any one of SEQ ID NO:17.
15

44. The polypeptide of claim 28 or 29, wherein the GR ligand binding domain has a crystalline structure further characterized by the atomic structure coordinates shown in Table 4.
20

45. The polypeptide of claim 28 or 29, wherein the crystalline form contains two GR α ligand binding domain polypeptide in the asymmetric unit.

25 46. The polypeptide of claim 28 or 29, wherein the crystalline form is such that the three-dimensional structure of the crystallized GR ligand binding domain polypeptide can be determined to a resolution of about 2.8 Å or better.

47. The polypeptide of claim 28 or 29, wherein the crystalline form contains one or more atoms having a molecular weight of 40 grams/mol or greater.
30

48. A method for determining the three-dimensional structure of a crystallized GR ligand binding domain polypeptide to a resolution of about 2.8 Å or better, the method comprising:

- (a) crystallizing a GR ligand binding domain polypeptide; and
- 5 (b) analyzing the GR ligand binding domain polypeptide to determine the three-dimensional structure of the crystallized GR ligand binding domain polypeptide, whereby the three-dimensional structure of a crystallized GR ligand binding domain polypeptide is determined to a resolution of about 2.8 Å or better.

10

49. The method of claim 48, wherein the analyzing is by X-ray diffraction.

50. The method of claim 48, wherein the crystallization is accomplished
15 by the hanging drop method, and wherein the GR ligand binding domain is mixed with a reservoir.

51. The method of claim 50, wherein the reservoir comprises 50mM HEPES, pH 7.5-8.5, and 1.7-2.3M ammonium formate.

20

52. The method of claim 48, wherein the crystallizing further comprises crystallizing the GR α ligand binding domain with a ligand and a peptide.

53. The method of claim 52, wherein the ligand is a steroid.

25

54. The method of claim 53, wherein the ligand is dexamethasone.

55. The method of claim 52, wherein the ligand is a steroid and the peptide is a fragment of a co-activator.

30

56. The method of claim 52, wherein the ligand is a steroid and the peptide is a fragment of a co-repressor.

57. The method of claim 52, wherein the ligand is dexamethasone and the peptide comprises an LXXLL (SEQ ID NO:18) motif.

5 58. The method of claim 52, wherein the peptide is a fragment of a TIF2 protein.

59. The method of claim 52, wherein the ligand is dexamethasone and the peptide has the amino acid sequence shown in SEQ ID NO:17.
10

60. A method of generating a crystallized GR ligand binding domain polypeptide, the method comprising:

- (a) incubating a solution comprising a GR ligand binding domain with a reservoir; and
- 15 (b) crystallizing the GR ligand binding domain polypeptide using the hanging drop method, whereby a crystallized GR ligand binding domain polypeptide is generated.

61. The method of claim 60, wherein the incubating further comprises
20 incubating the GR ligand binding domain with a ligand and a peptide.

62. The method of claim 61, wherein the ligand is a steroid.

63. The method of claim 62, wherein the steroid is dexamethasone.
25

64. The method of claim 61, wherein the ligand is a steroid and the peptide is a fragment of a co-activator.

65. The method of claim 61, wherein the ligand is a steroid and the
30 peptide is a fragment of a co-repressor.

66. The method of claim 61, wherein the ligand is dexamethasone and the peptide comprises an LXXLL (SEQ ID NO:18) motif.

67. The method of claim 61, wherein the peptide is a fragment of a TIF2 protein.

5 68. A crystallized GR α ligand binding domain polypeptide produced by the method of claim 60.

69. A method of designing a modulator of a nuclear receptor, the method comprising:

- 10 (a) designing a potential modulator of a nuclear receptor that will make interactions with amino acids in the ligand binding site of the nuclear receptor based upon the atomic structure coordinates of a GR ligand binding domain polypeptide;
- (b) synthesizing the modulator; and
- 15 (c) determining whether the potential modulator modulates the activity of the nuclear receptor, whereby a modulator of a nuclear receptor is designed.

20 70. The method of claim 69, wherein the atomic structure coordinates further comprises a ligand and a peptide bound to the GR ligand binding domain polypeptide.

25 71. The method of claim 69, wherein the atomic structure coordinates are the atomic structural coordinates shown in Table 3.

72. The method of claim 70, wherein the ligand is a steroid.

73. The method of claim 72, wherein the steroid is dexamethasone.

30 74. The method of claim 70, wherein the ligand is a steroid and the peptide is a fragment of a co-activator.

75. The method of claim 70, wherein the ligand is a steroid and the peptide is a fragment of a co-repressor.

76. The method of claim 70, wherein the ligand is dexamethasone and
5 the peptide comprises an LXXLL (SEQ ID NO:18) motif.

77. The method of claim 70, wherein the peptide is a fragment of a TIF2 protein.

10 78. A method of designing a modulator that selectively modulates the activity of a GR α polypeptide the method comprising:

- (a) obtaining a crystalline form of a GR α ligand binding domain polypeptide;
- (b) determining the three-dimensional structure of the crystalline form of
15 the GR α ligand binding domain polypeptide; and
- (c) synthesizing a modulator based on the three-dimensional structure of the crystalline form of the GR α ligand binding domain polypeptide, whereby a modulator that selectively modulates the activity of a GR α polypeptide is designed.

20 79. The method of claim 78, wherein the method further comprises contacting a GR α ligand binding domain polypeptide with the potential modulator; and assaying the GR α ligand binding domain polypeptide for binding of the potential modulator, for a change in activity of the GR α ligand binding domain
25 polypeptide, or both.

80. The method of claim 78, wherein the crystalline form is a hexagonal form.

30 81. The method of claim 80, wherein the crystals are such that the three-dimensional structure of the crystallized GR α ligand binding domain polypeptide can be determined to a resolution of about 2.8 Å or better.

82. The method of claim 78, wherein the crystalline form comprises a GR α ligand binding domain with a ligand and a peptide.

5 83. The method of claim 82, wherein the ligand is a steroid.

84. The method of claim 83, wherein the steroid is dexamethasone.

10 85. The method of claim 82, wherein the ligand is a steroid and the peptide is a fragment of a co-activator.

86. The method of claim 82, wherein the ligand is a steroid and the peptide is a fragment of a co-repressor.

15 87. The method of claim 82, wherein the ligand is dexamethasone and the peptide comprises an LXXLL (SEQ ID NO:18) motif.

88. The method of claim 82, wherein the peptide is a fragment of a TIF2 protein.

20

89. The method of claim 78, wherein the three-dimensional structure of the crystalline form of the GR α ligand binding domain polypeptide is described by the atomic coordinates shown in Table 4.

25 90. A method of screening a plurality of compounds for a modulator of a GR ligand binding domain polypeptide, the method comprising:

- (a) providing a library of test samples;
- (b) contacting a GR ligand binding domain polypeptide with each test sample;
- 30 (c) detecting an interaction between a test sample and the GR ligand binding domain polypeptide;
- (d) identifying a test sample that interacts with the GR ligand binding domain polypeptide; and

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- (e) isolating a test sample that interacts with the GR ligand binding domain polypeptide, whereby a plurality of compounds is screened for a modulator of a GR ligand binding domain polypeptide.

5 91. The method of claim 90, wherein the test samples are bound to a substrate.

 92. The method of claim 90, wherein the test samples are synthesized directly on a substrate.

10

 93. A method for identifying a GR modulator, the method comprising:

- (a) providing atomic coordinates of a GR ligand binding domain to a computerized modeling system; and

15

- (b) modeling ligands that fit spatially into the binding pocket of the GR ligand binding domain to thereby identify a GR modulator, whereby a GR modulator is identified.

 94. The method of claim 93, wherein the method further comprises identifying in an assay for GR-mediated activity a modeled ligand that increases or
20 decreases the activity of the GR.

 95. The method of claim 93, wherein the atomic coordinates are the atomic coordinates shown in Table 4.

 96. A method of identifying modulator that selectively modulates the
25 activity of a GR α polypeptide compared to other GR polypeptides, the method comprising:

- (a) providing atomic coordinates of a GR α ligand binding domain to a computerized modeling system; and

30

- (b) modeling a ligand that fits into the binding pocket of a GR α ligand binding domain and that interacts with conformationally constrained residues of a GR α conserved among GR subtypes, whereby a modulator that selectively modulates the activity of a GR α polypeptide compared to other polypeptides is identified.

97. The method of claim 96, wherein the method further comprises identifying in a biological assay for GR activity a modeled ligand that selectively binds to GR α and increases or decreases the activity of said GR α .

5

98. The method of claim 96, wherein the atomic coordinates are the atomic coordinates shown in Table 4.

99. A method of designing a modulator of a GR polypeptide, the method comprising:

10

- (a) selecting a candidate GR ligand;
- (b) determining which amino acid or amino acids of a GR polypeptide interact with the ligand using a three-dimensional model of a crystallized protein comprising a GR α LBD;

15

- (c) identifying in a biological assay for GR activity a degree to which the ligand modulates the activity of the GR polypeptide;
- (d) selecting a chemical modification of the ligand wherein the interaction between the amino acids of the GR polypeptide and the ligand is predicted to be modulated by the chemical modification;

20

- (e) synthesizing a chemical compound with the selected chemical modification to form a modified ligand;
- (f) contacting the modified ligand with the GR polypeptide;

- (g) identifying in a biological assay for GR activity a degree to which the modified ligand modulates the biological activity of the GR polypeptide; and

25

- (h) comparing the biological activity of the GR polypeptide in the presence of modified ligand with the biological activity of the GR polypeptide in the presence of the unmodified ligand, whereby a modulator of a GR polypeptide is designed.

30

100. The method of claim 99, wherein the GR polypeptide is a GR α polypeptide.

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101. The method of claim 99, wherein the three-dimensional model of a crystallized protein is a GR α ligand binding domain with a ligand and a peptide.

102. The method of claim 101, wherein the ligand is a steroid.

103. The method of claim 101, wherein the steroid is dexamethasone.

104. The method of claim 101, wherein the ligand is a steroid and the peptide is a fragment of a co-activator.

105. The method of claim 101, wherein the ligand is a steroid and the peptide is a fragment of a co-repressor.

106. The method of claim 101, wherein the ligand is dexamethasone and the peptide comprises an LXXLL (SEQ ID NO:18) motif.

107. The method of claim 101, wherein the peptide is a fragment of a TIF2 protein.

108. The method of claim 99, wherein the three-dimensional model is represented by the three dimensional coordinates shown in Table 4.

109. The method of claim 99, wherein the method further comprises repeating steps (a) through (f), if the biological activity of the GR polypeptide in the presence of the modified ligand varies from the biological activity of the GR polypeptide in the presence of the unmodified ligand.

110. An assay method for identifying a compound that inhibits binding of a ligand to a GR polypeptide, the assay method comprising:

- (a) designing a test inhibitor compound based on the three dimensional atomic coordinates of GR;
- (b) incubating a GR polypeptide with a ligand in the presence of a test

inhibitor compound;

(c) determining an amount of ligand that is bound to the GR polypeptide, wherein decreased binding of ligand to the GR protein in the presence of the test inhibitor compound relative to binding of ligand in the absence of the test inhibitor compound is indicative of inhibition; and

(d) identifying the test compound as an inhibitor of ligand binding if decreased ligand binding is observed, whereby a compound that inhibits binding of a ligand to a GR polypeptide is identified.

111. The method of claim 110, wherein the ligand is a steroid.

112. The method of claim 111, wherein the steroid is dexamethasone.

113. The method of claim 110, wherein the three dimensional coordinates are the three dimensional coordinates shown in Table 4.

114. A method of identifying a NR modulator that selectively modulates the biological activity of one NR compared to GR α , the method comprising:

(a) providing an atomic structure coordinate set describing a GR α ligand binding domain structure and at least one other atomic structure coordinate set describing a NR ligand binding domain, each ligand binding domain comprising a ligand binding site;

(b) comparing the atomic structure coordinate sets to identify at least one difference between the sets;

(c) designing a candidate ligand predicted to interact with the difference of step (b);

(d) synthesizing the candidate ligand; and

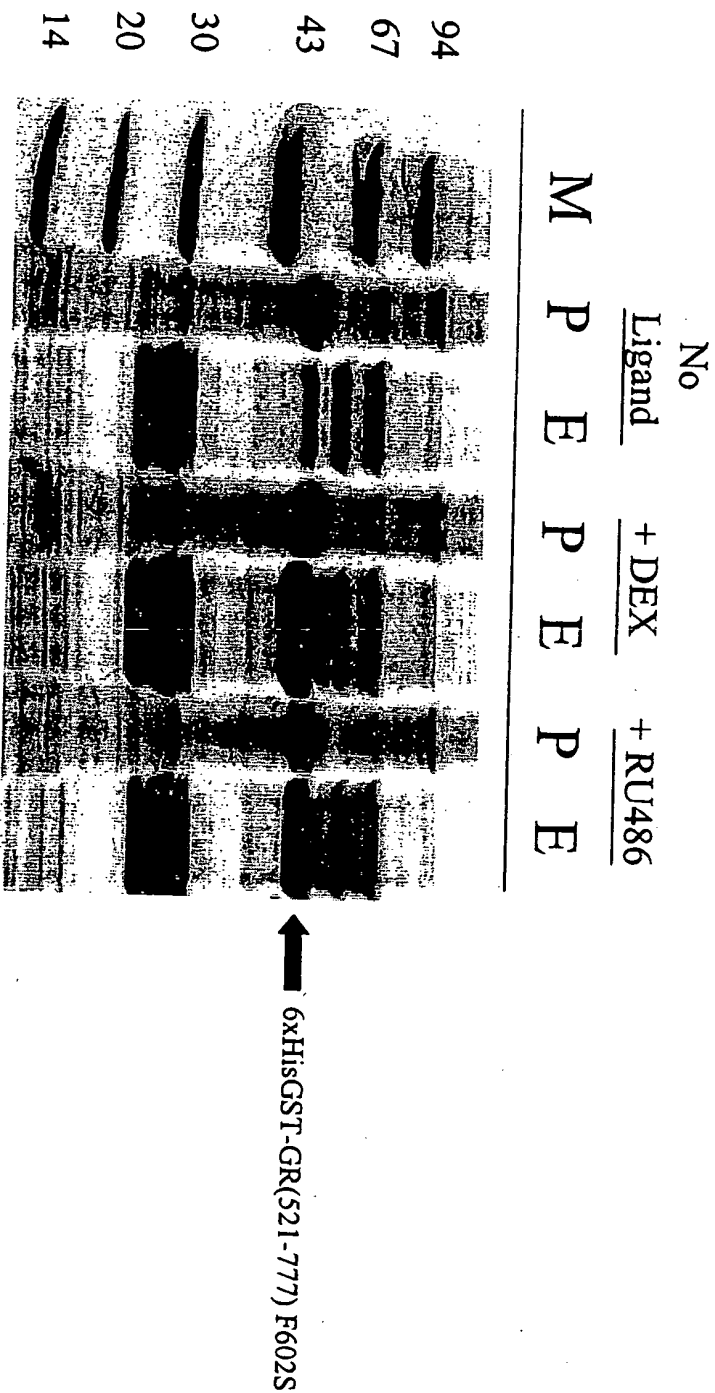
(e) testing the synthesized candidate ligand for an ability to selectively modulate a NR as compared to GR α , whereby a NR modulator that selectively modulates the biological activity NR compared to GR α is identified.

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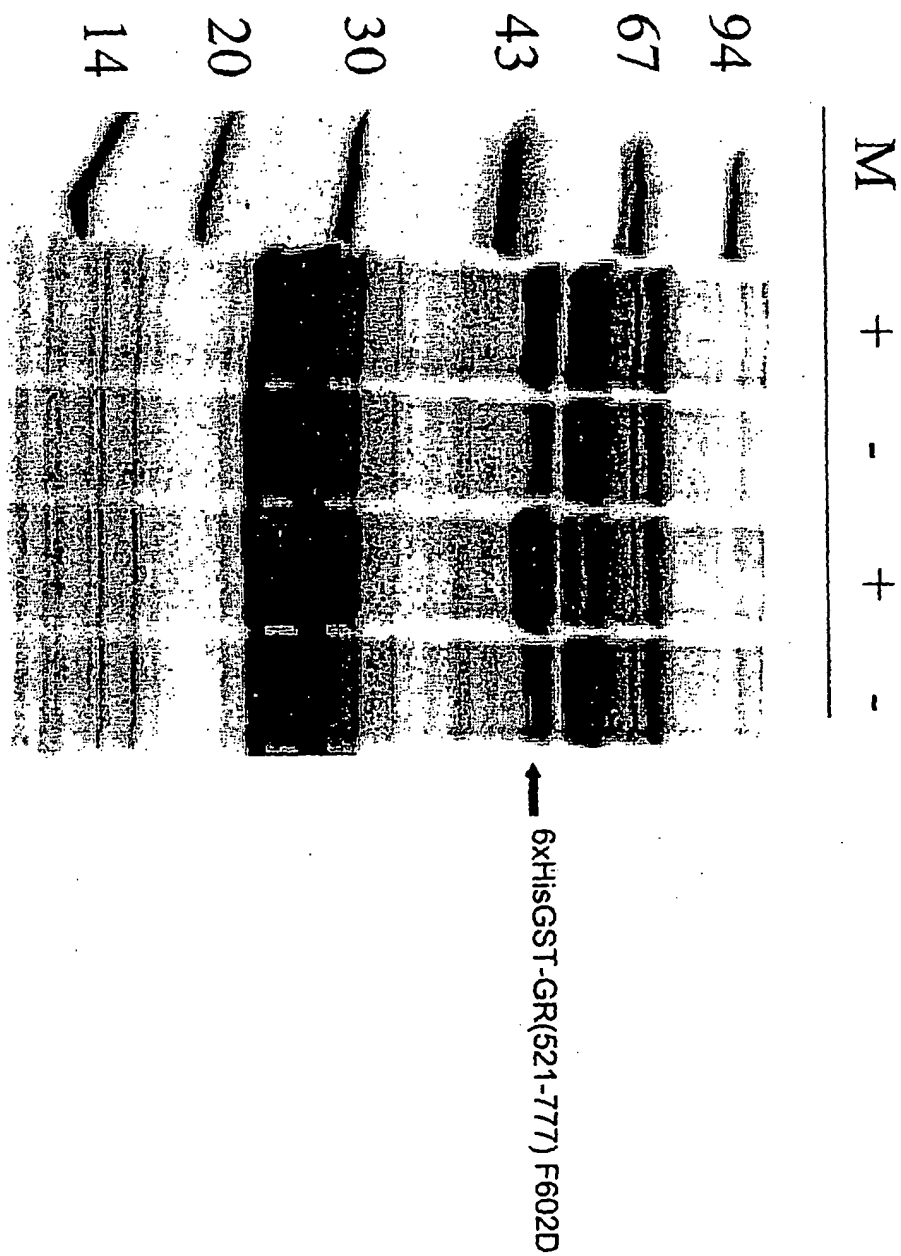
115. The method of claim 114, wherein the GR α atomic structure coordinate set is the atomic structure coordinate set shown in Table 4.

116. The method of claim 114, wherein the NR is selected from the group
5 consisting of MR, PR, AR, GR β and isoforms thereof that have ligands that also bind GR α .

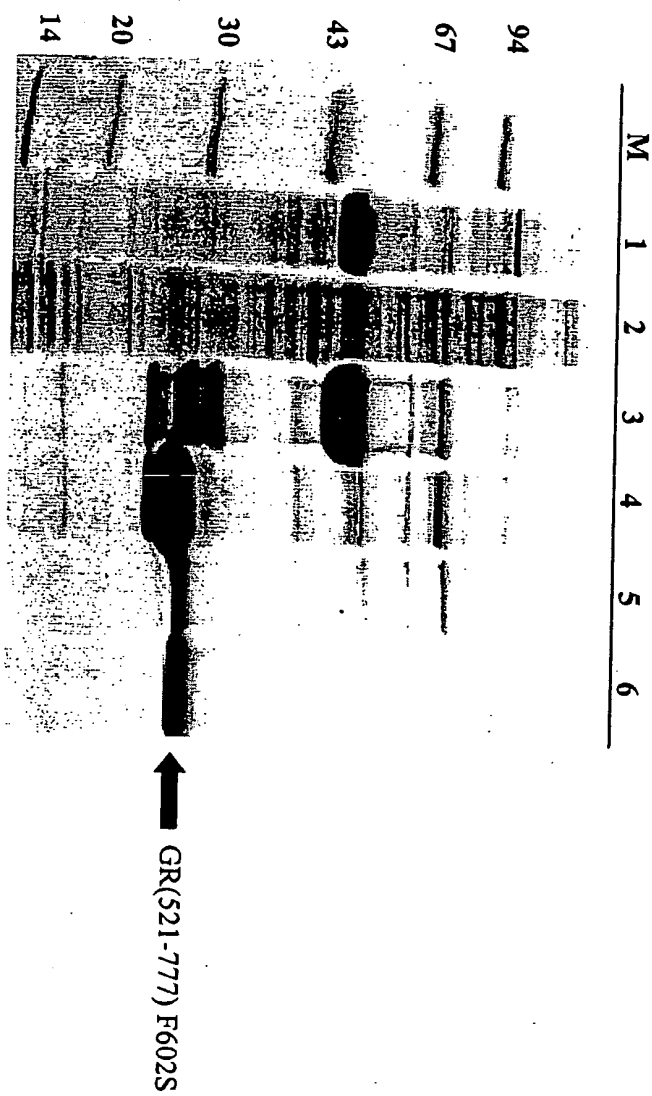
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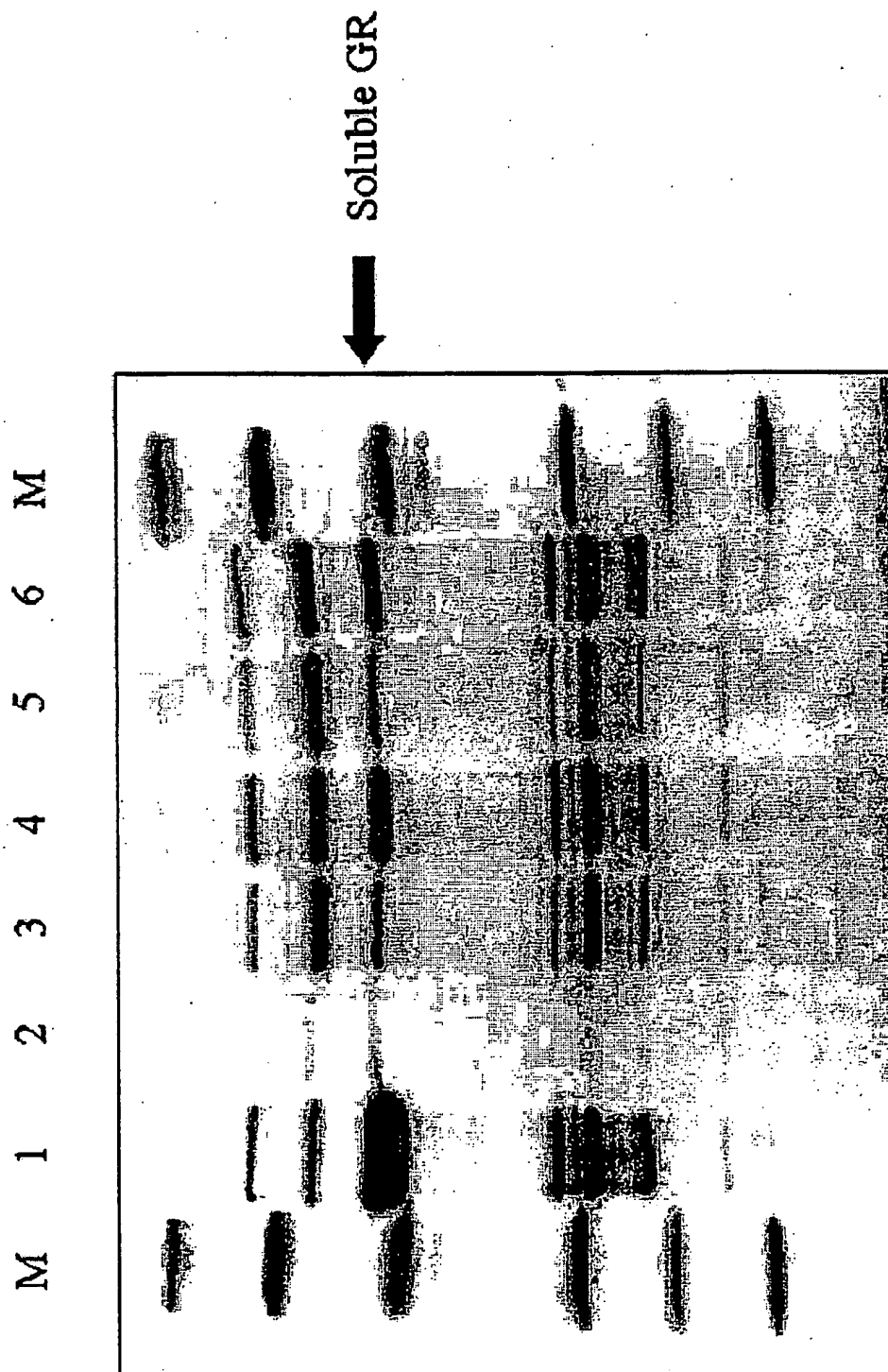
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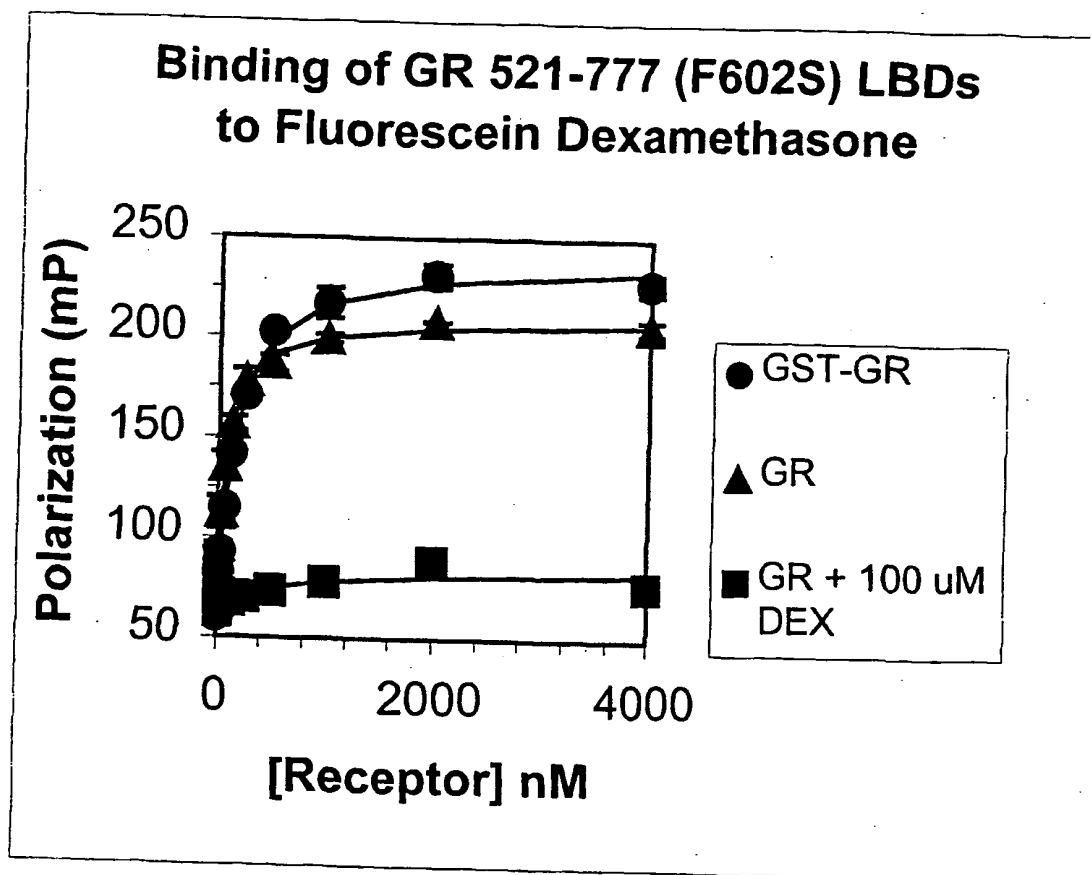
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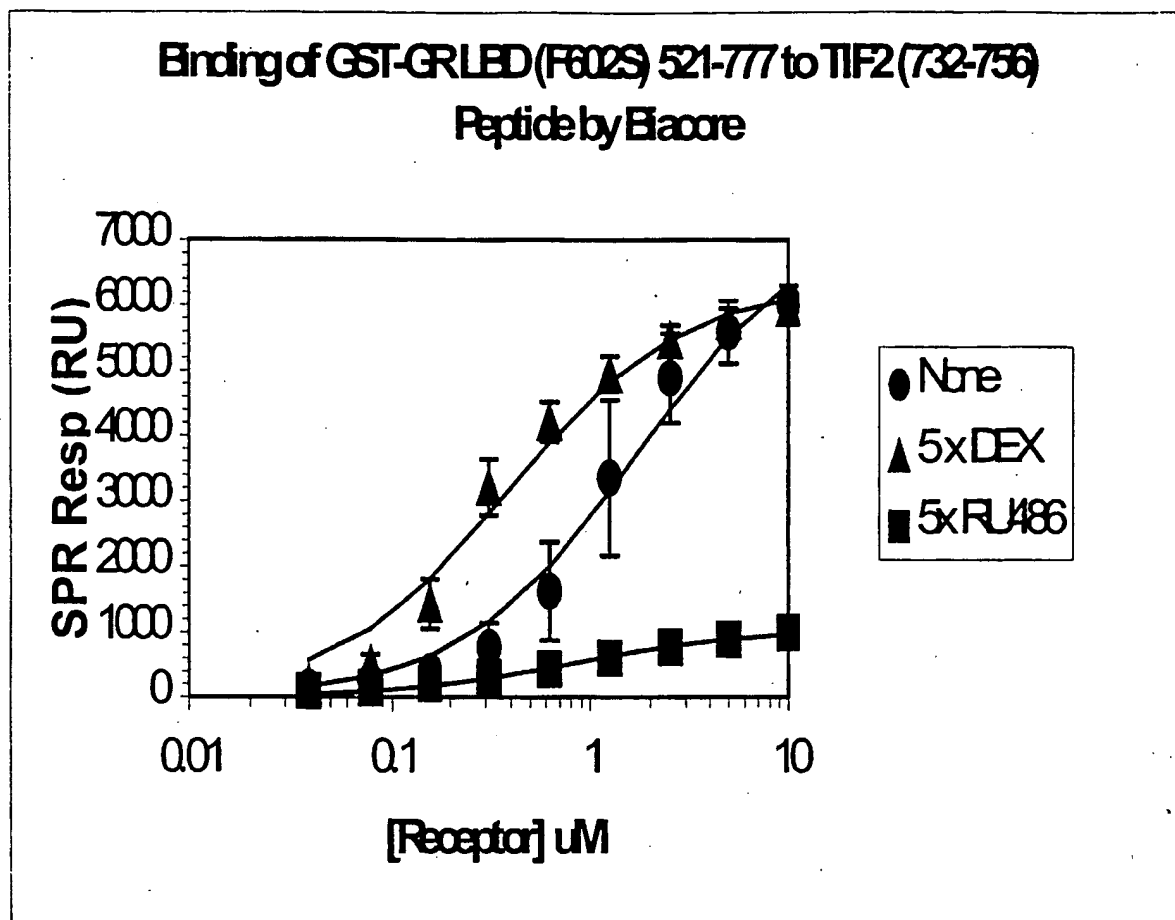
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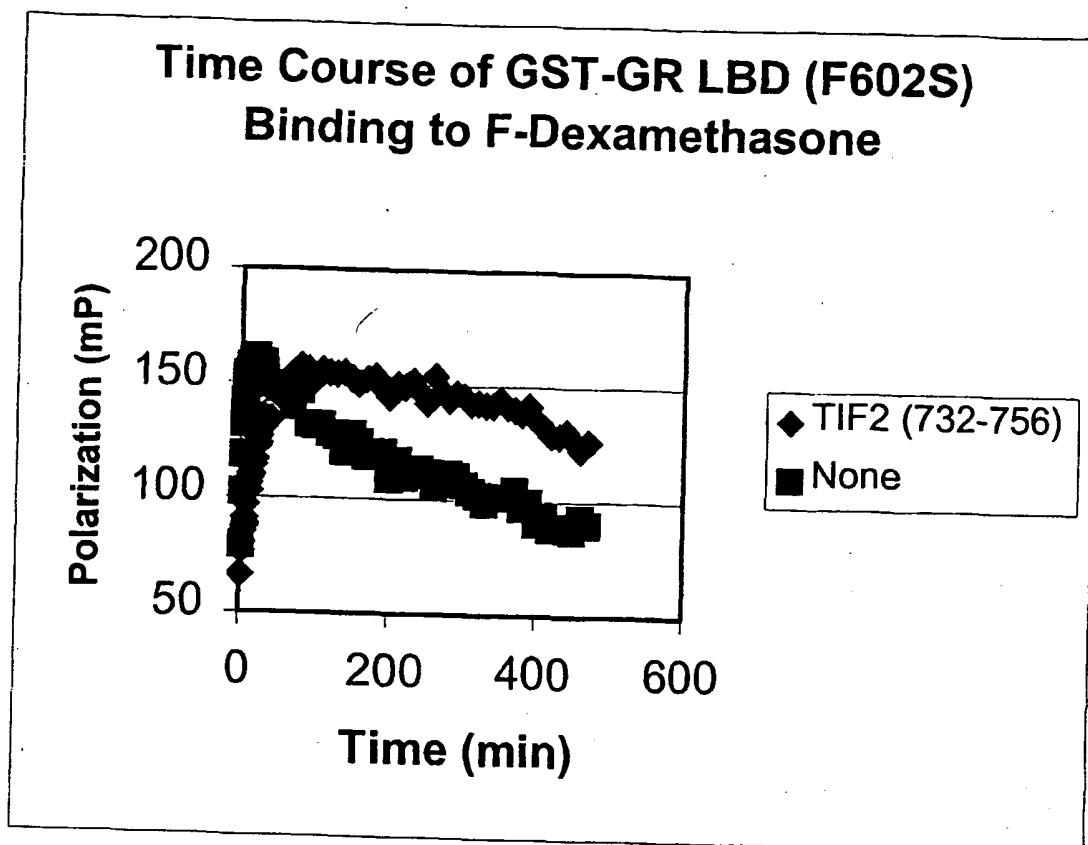
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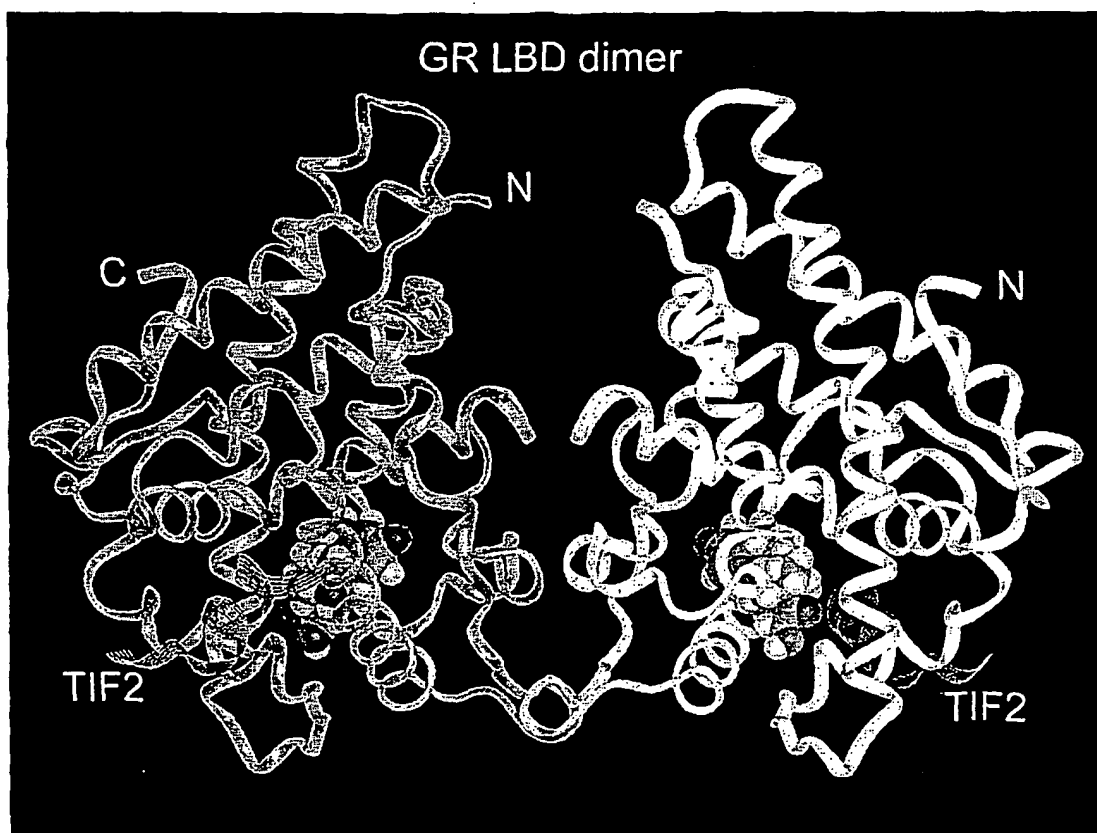
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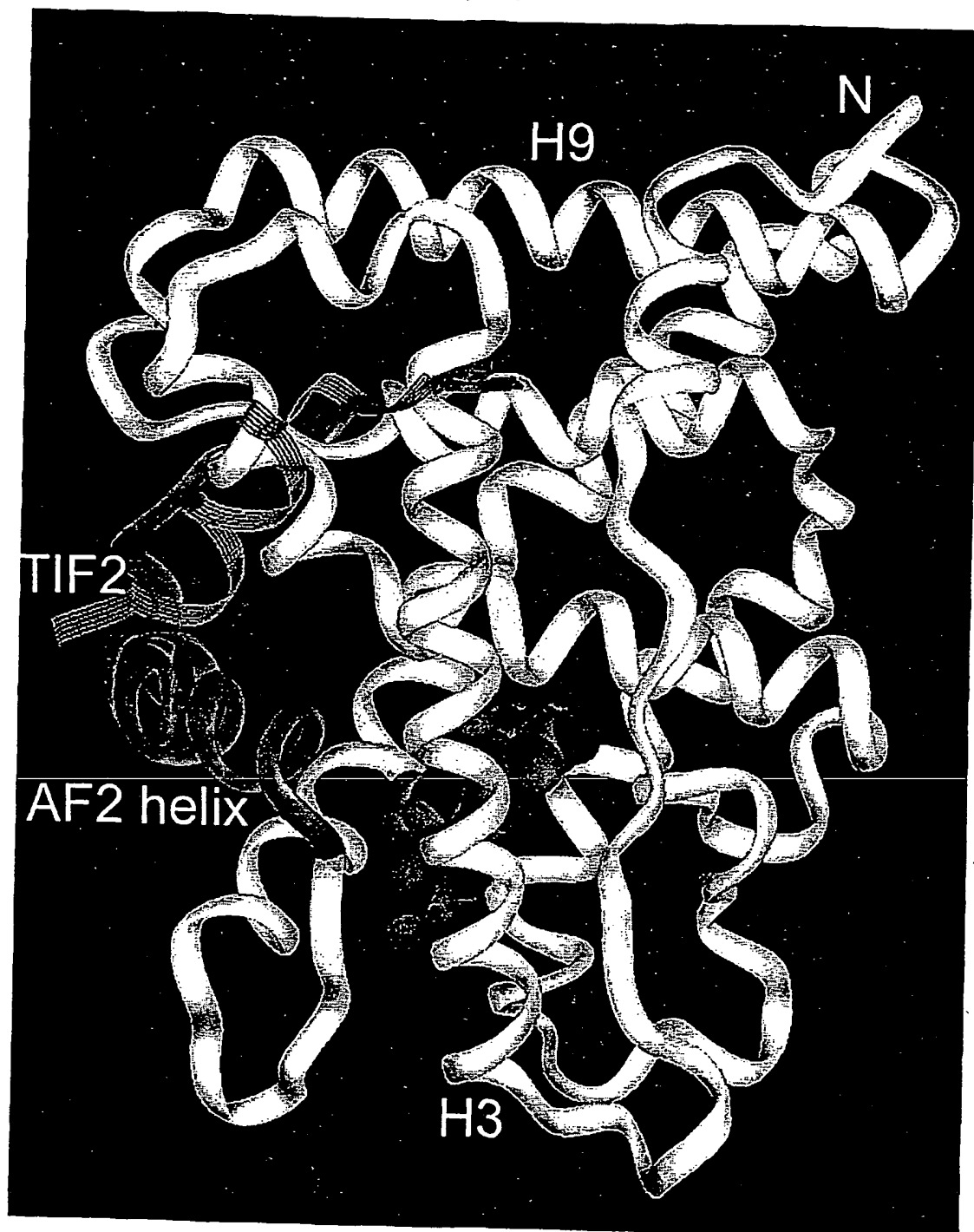
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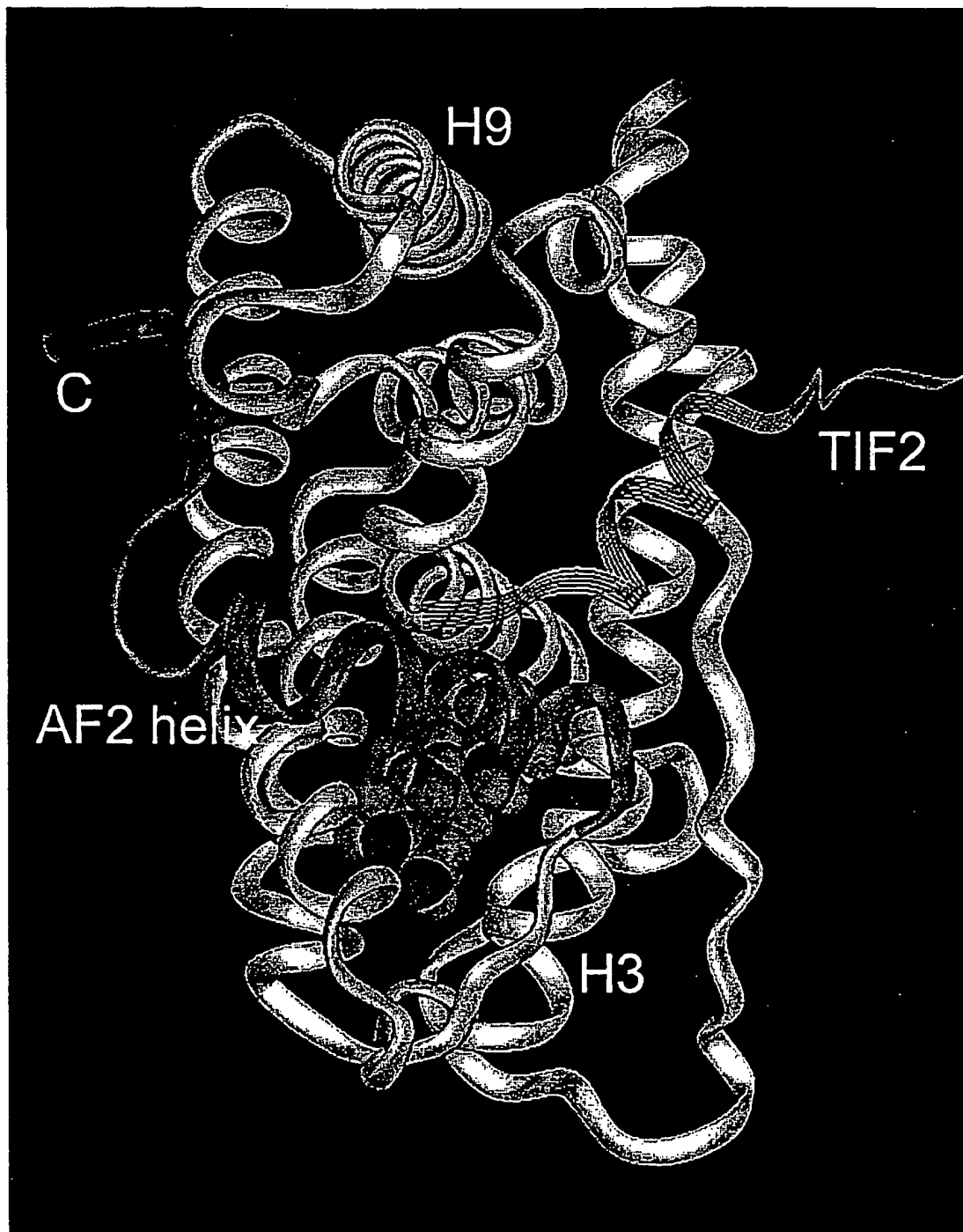
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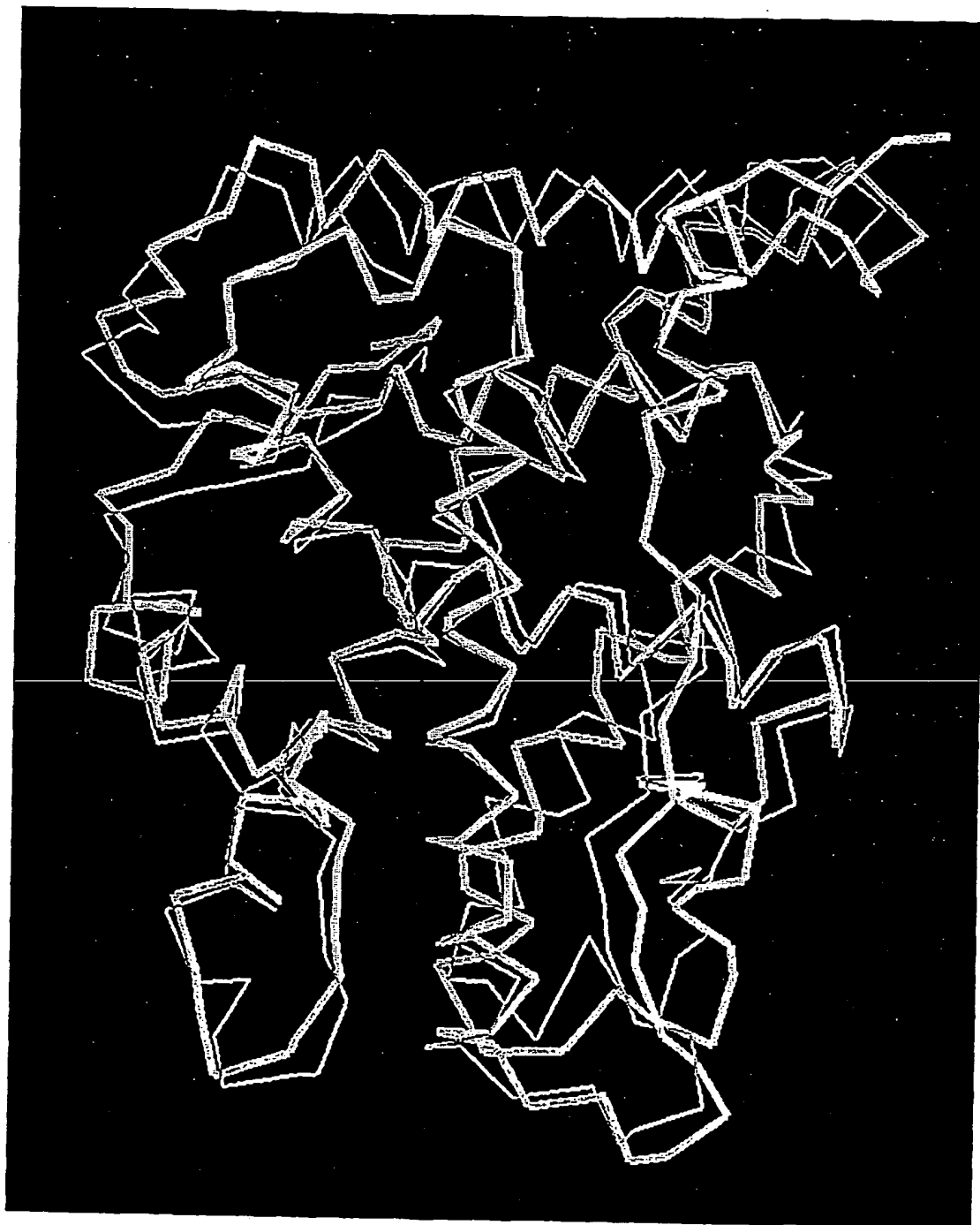
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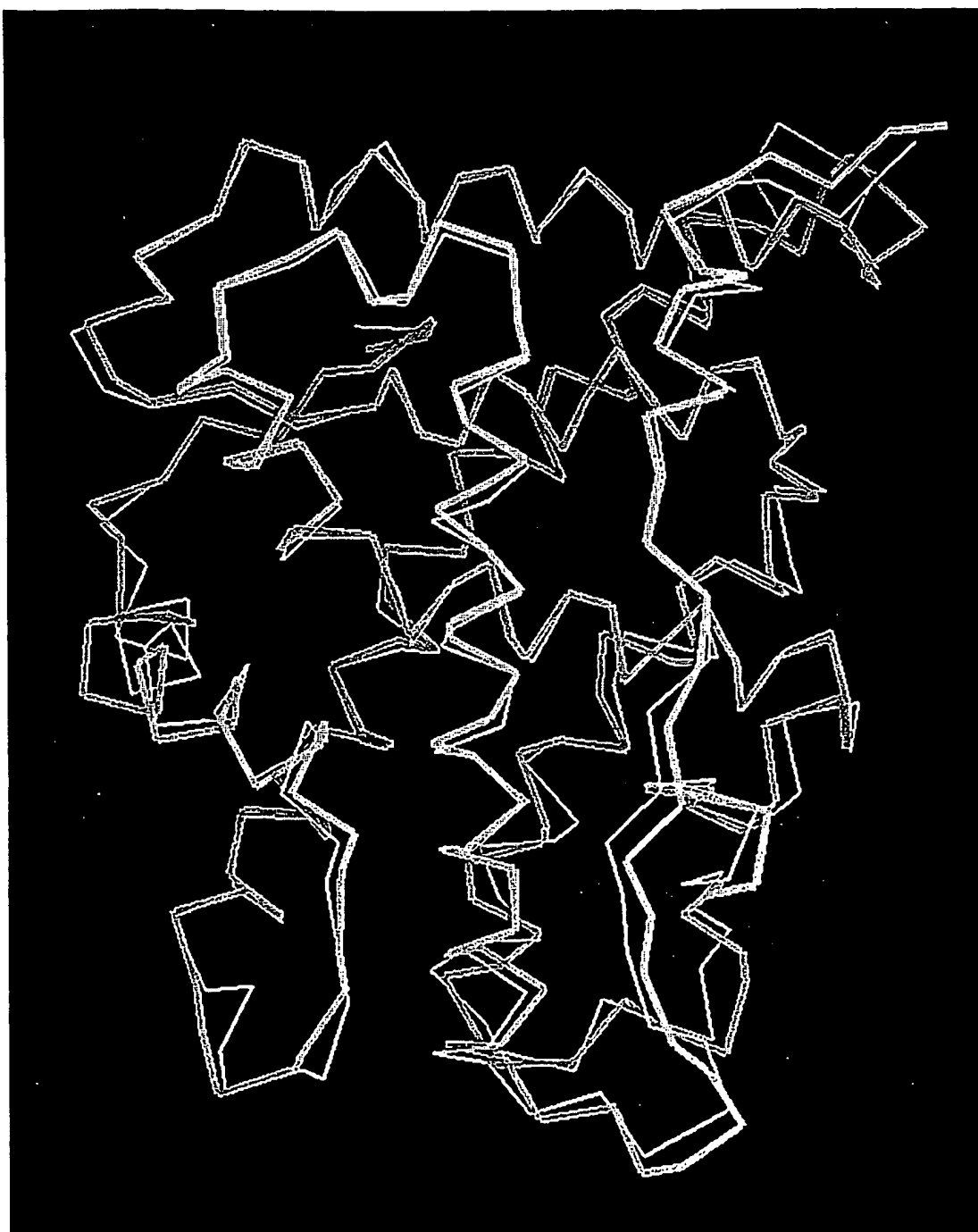
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GR 527 QLTPTLVSLLEVI EPEVLYAGYDSSVPDS TWRIIMTTLNMLGGRQV
MR 733 ALTPSPVMVLENI EPEIVYAGYDSSKPD TAENLLSTLNRLAGQM
PR 682 QLIPPLINLLMSI EPDVIYAGHDNTKPD TSSSLLTSLNQLGERQL
AR 668 ECQPIFLNVLEAI EPGVVCAGHDNNQPD FAALLSSSLNELGERQL
ERA 310 LTADQMVSALLDAEPPILYSEYDPTRPFS EASMMGLLTNLADREL
ERB 263 LSP EQLVLTLLLEA EPPHVLIS - RPSAPFT EASMMMSLTKLADKEL
helix-1 helix-3

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ERB 307 VHMISWAKKIPGFVELSLFDQVRLLES CWMEVLMMLGWMWRSIDH-
helix-3' helix-4 helix-5

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PR 772 SGQMLYFAPDLILNEQRMK-ESSFYSLCLTMWQIPQEFVKLQVSSQ
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beta-3 beta-4 helix-6 helix-7

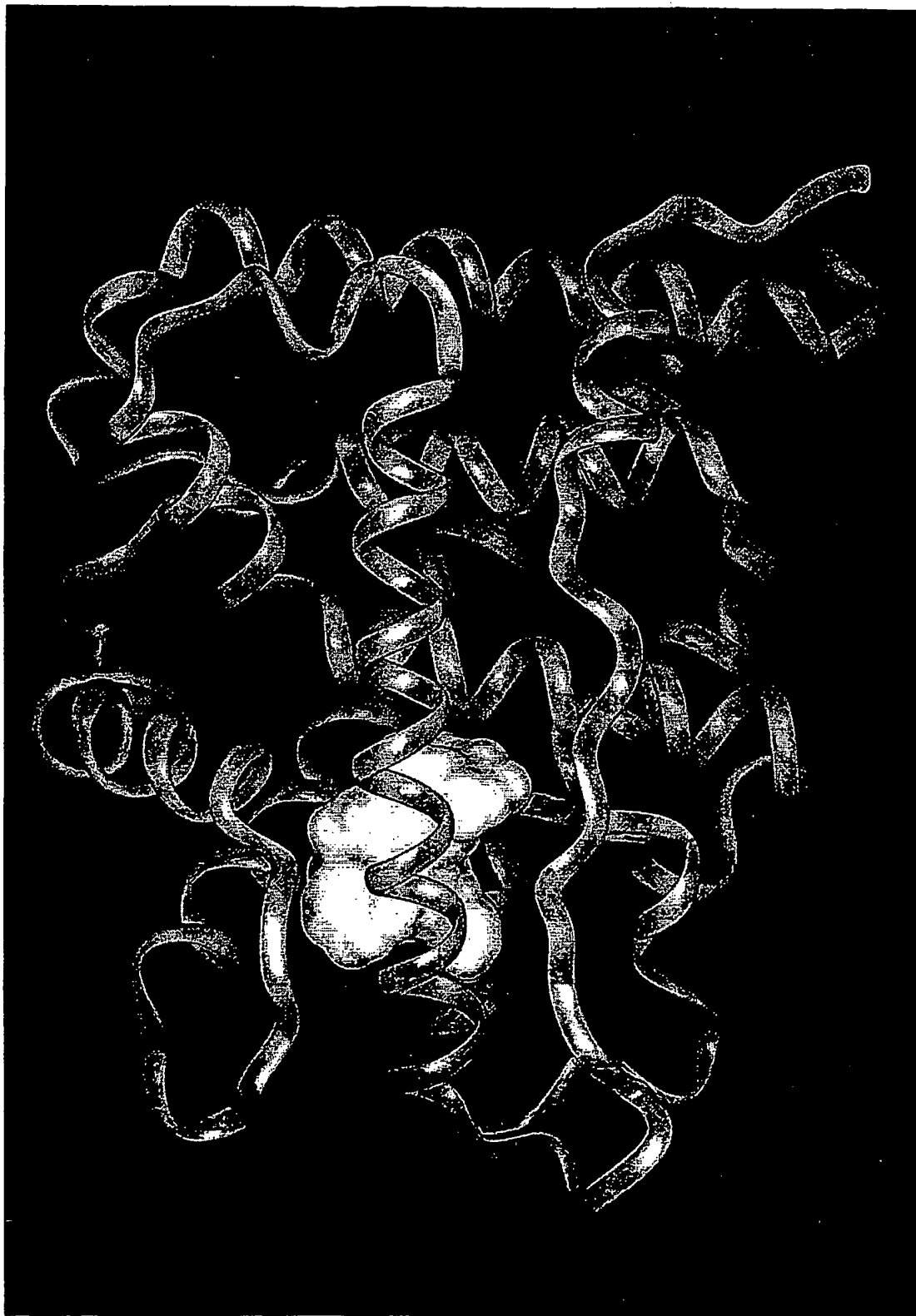
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AR 802 QEFLCMKAL LLS - - - - - IIPVDGLKNQKFFDELRMNYIKELD
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ERB 395 KEYLCVKAMIL LNS SMYPLV - TATQDADSSRKLALHLLNAVTDALV
helix-8 beta-5 helix-9

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helix-10

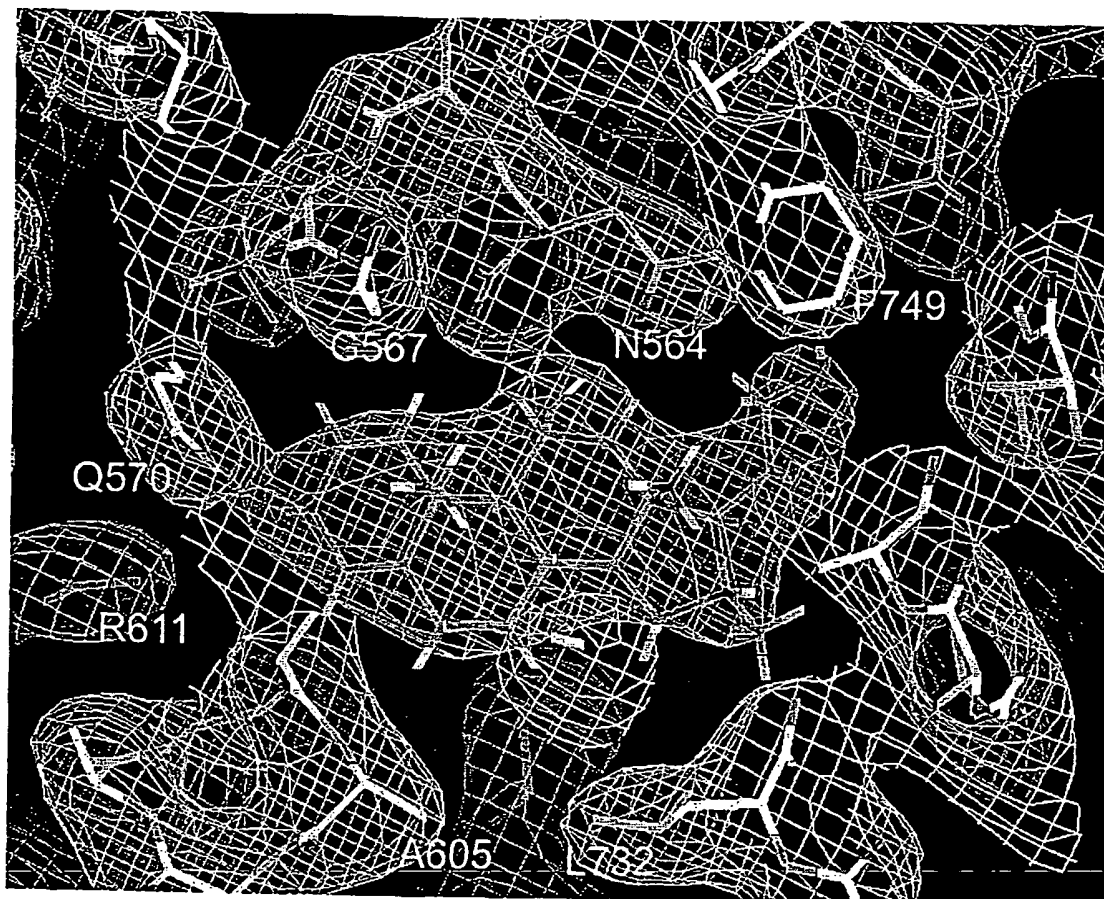
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ERA 533 - - - VVPLYD LLLLEMLDAHRLHAPTSRGGASVEETDQSHLATAGST
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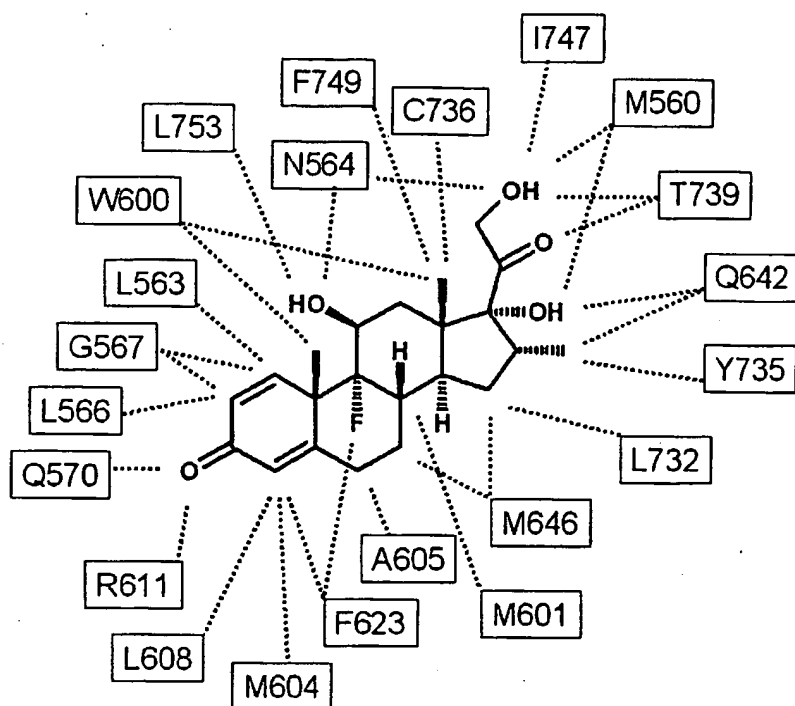
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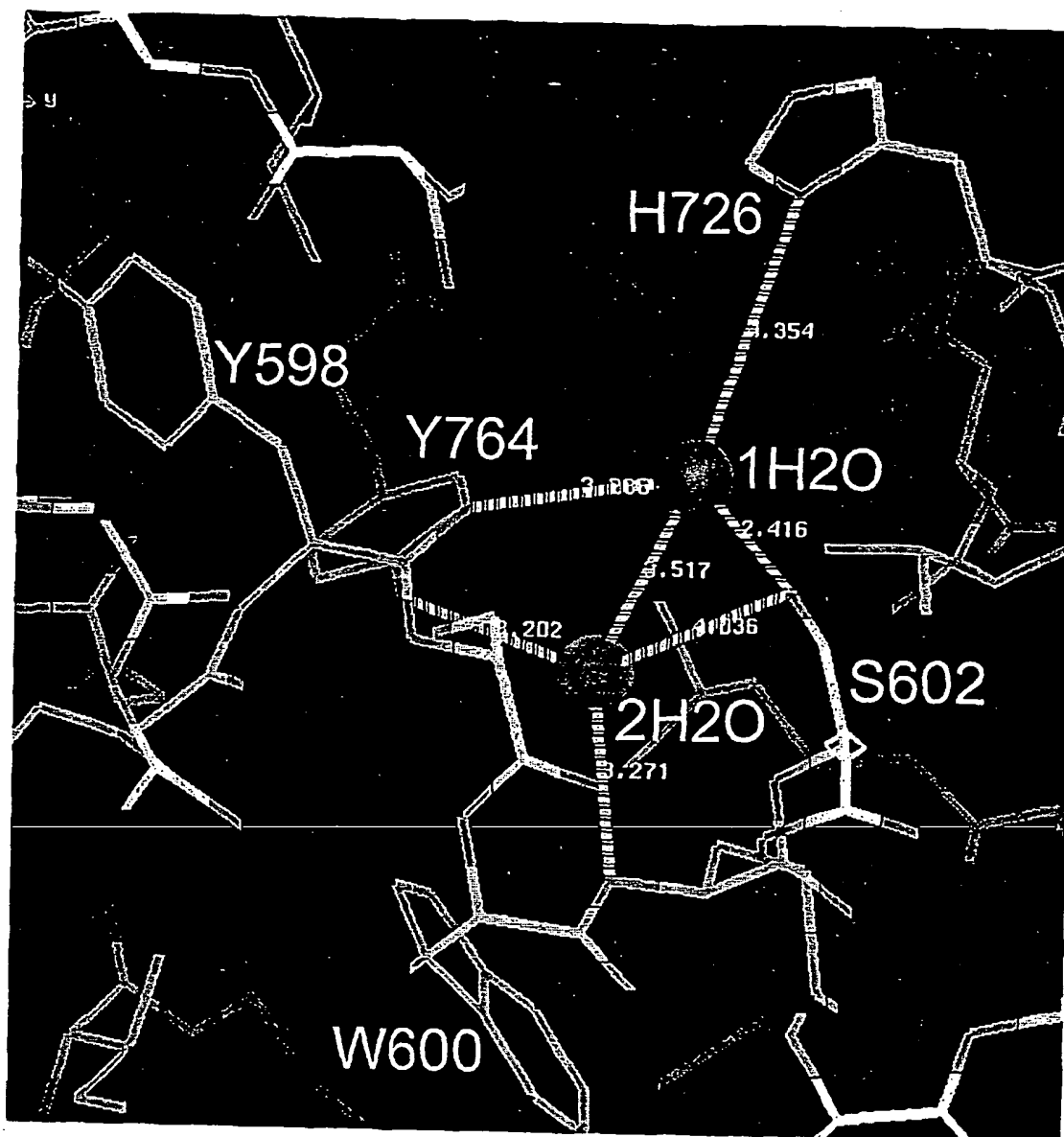
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SEQUENCE LISTING

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<120> CRYSTALLIZED GLUCOCORTICOID RECEPTOR LIGAND BINDING DOMAIN POLYPEPTIDE AND SCREENING METHODS EMPLOYING SAME

<130> Docket No. PU4523

<140>

<141>

<150> 60/305,902

<151> 2001-07-17

<160> 41

<170> PatentIn version 3.1

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Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser 305 310 315 320		
Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met 325 330 335		
Asn Thr Ala Ser Leu Ser Gln Gln Gln Asp Gln Lys Pro Ile Phe Asn 340 345 350		
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tgg gca aag gca ata cca ggt ttc agg aac tta cac ctg gat gac caa Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln 580 585 590			1776
atg acc cta ctg cag tac tcc tgg atg tcc ctt atg gca ttt gct ctg Met Thr Leu Leu Gln Tyr Ser Trp Met Ser Leu Met Ala Phe Ala Leu 595 600 605			1824
ggg tgg aga tca tat aga caa tca agt gca aac ctg ctg tgt ttt gct Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala 610 615 620			1872
cct gat ctg att att aat gag cag aga atg act cta ccc tgc atg tac Pro Asp Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Cys Met Tyr 625 630 635 640			1920
gac caa tgt aaa cac atg ctg tat gtt tcc tct gag tta cac agg ctt Asp Gln Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu 645 650 655			1968
cag gta tct tat gaa gag tat ctc tgt atg aaa acc tta ctg ctt ctc Gln Val Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu 660 665 670			2016
tct tca gtt cct aag gac ggt ctg aag agc caa gag cta ttt gat gaa Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu 675 680 685			2064
att aga atg acc tac atc aaa gag cta gga aaa gcc att gtc aag agg Ile Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg 690 695 700			2112
gaa gga aac tcc agc cag aac tgg cag cgg ttt tat caa ctg aca aaa Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys 705 710 715 720			2160

ctc ttg gat tct atg cat gaa gtg gtt gaa aat ctc ctt aac tat tgc 2208
 Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys
 725 730 735

ttc caa aca ttt ttg gat aag acc atg agt att gaa ttc ccc gag atg 2256
 Phe Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met
 740 745 750

tta gct gaa atc atc acc aat cag ata cca aaa tat tca aat gga aat 2304
 Leu Ala Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn
 755 760 765

atc aaa aaa ctt ctg ttt cat caa aag tga 2334
 Ile Lys Lys Leu Leu Phe His Gln Lys
 770 775

<210> 4

<211> 777

<212> PRT

<213> Homo sapiens

<400> 4

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Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr
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Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu
 35 40 45

Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp
 50 55 60

Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys
 65 70 75 80

Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys
 85 90 95

Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu
 100 105 110

Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn
 115 120 125

Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser
 130 135 140

Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His
 145 150 155 160

Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr
 165 170 175

Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp
 180 185 190

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Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr
 195 200 205
 Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu
 210 215 220
 Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn
 225 230 235 240
 Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys
 245 250 255
 Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr
 260 265 270
 Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr
 275 280 285
 Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala
 290 295 300
 Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser
 305 310 315 320
 Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met
 325 330 335
 Asn Thr Ala Ser Leu Ser Gln Gln Gln Asp Gln Lys Pro Ile Phe Asn
 340 345 350
 Val Ile Pro Pro Ile Pro Val Gly Ser Glu Asn Trp Asn Arg Cys Gln
 355 360 365
 Gly Ser Gly Asp Asp Asn Leu Thr Ser Leu Gly Thr Leu Asn Phe Pro
 370 375 380
 Gly Arg Thr Val Phe Ser Asn Gly Tyr Ser Ser Pro Ser Met Arg Pro
 385 390 395 400
 Asp Val Ser Ser Pro Pro Ser Ser Ser Ser Thr Ala Thr Thr Gly Pro
 405 410 415
 Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His
 420 425 430
 Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala
 435 440 445
 Val Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp Cys Ile
 450 455 460
 Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Tyr Arg Lys
 465 470 475 480
 Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys Lys Lys
 485 490 495

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Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr Ser
500 505 510

Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Leu Pro Gln Leu
515 520 525

Thr Pro Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu
530 535 540

Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile Met
545 550 555 560

Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys
565 570 575

Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln
580 585 590

Met Thr Leu Leu Gln Tyr Ser Trp Met Ser Leu Met Ala Phe Ala Leu
595 600 605

Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala
610 615 620

Pro Asp Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Cys Met Tyr
625 630 635 640

Asp Gln Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu
645 650 655

Gln Val Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu
660 665 670

Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu
675 680 685

Ile Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg
690 695 700

Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys
705 710 715 720

Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys
725 730 735

Phe Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met
740 745 750

Leu Ala Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn
755 760 765

Ile Lys Lys Leu Leu Phe His Gln Lys
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<211> 2334

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(2334)

<223>

<400> 5

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agt gtg ctt gct cag gag agg gga gat gtg atg gac ttc tat aaa acc	96
Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr	
20 25 30	
cta aga gga gga gct act gtg aag gtt tct gcg tct tca ccc tca ctg	144
Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu	
35 40 45	
gct gtc gct tct caa tca gac tcc aag cag cga aga ctt ttg gtt gat	192
Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp	
50 55 60	
ttt cca aaa ggc tca gta agc aat gcg cag cag cca gat ctg tcc aaa	240
Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys	
65 70 75 80	
gca gtt tca ctc tca atg gga ctg tat atg gga gag aca gaa aca aaa	288
Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys	
85 90 95	
gtg atg gga aat gac ctg gga ttc cca cag cag ggc caa atc agc ctt	336
Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu	
100 105 110	
tcc tcg ggg gaa aca gac tta aag ctt ttg gaa gaa agc att gca aac	384
Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn	
115 120 125	
ctc aat agg tcg acc agt gtt cca gag aac ccc aag agt tca gca tcc	432
Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser	
130 135 140	
act gct gtg tct gct gcc ccc aca gag aag gag ttt cca aaa act cac	480
Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His	
145 150 155 160	
tct gat gta tct tca gaa cag caa cat ttg aag ggc cag act ggc acc	528
Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr	
165 170 175	
aac ggt ggc aat gtg aaa ttg tat acc aca gac caa agc acc ttt gac	576
Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp	
180 185 190	
att ttg cag gat ttg gag ttt tct tct ggg tcc cca ggt aaa gag acg	624
Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr	
195 200 205	
aat gag agt cct tgg aga tca gac ctg ttg ata gat gaa aac tgt ttg	672
Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu	
210 215 220	
ctt tct cct ctg gcg gga gaa gac gat tca ttc ctt ttg gaa gga aac	720

Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn 225 230 235 240	
tcg aat gag gac tgc aag cct ctc att tta ccg gac act aaa ccc aaa Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys 245 250 255	768
att aag gat aat gga gat ctg gtt ttg tca agc ccc agt aat gta aca Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr 260 265 270	816
ctg ccc caa gtg aaa aca gaa aaa gaa gat ttc atc gaa ctc tgc acc Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr 275 280 285	864
cct ggg gta att aag caa gag aaa ctg ggc aca gtt tac tgt cag gca Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala 290 295 300	912
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ggt cga aca gtt ttt tct aat ggc tat tca agc ccc agc atg aga cca Gly Arg Thr Val Phe Ser Asn Gly Tyr Ser Ser Pro Ser Met Arg Pro 385 390 395 400	1200
gat gta agc tct cct cca tcc agc tcc tca aca gca aca aca gga cca Asp Val Ser Ser Pro Pro Ser Ser Ser Thr Ala Thr Thr Gly Pro 405 410 415	1248
cct ccc aaa ctc tgc ctg gtg tgc tct gat gaa gct tca gga tgt cat Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His 420 425 430	1296
tat gga gtc tta act tgt gga agc tgt aaa gtt ttc ttc aaa aga gca Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala 435 440 445	1344
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ata aaa gga att cag cag gcc act aca gga gtc tca caa gaa acc tct Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr Ser 500 505 510	1536
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acc cct acc ctg gtg tca ctg ttg gag gtt att gaa cct gaa gtg tta	1632

Thr	Pro	Thr	Leu	Val	Ser	Leu	Leu	Glu	Val	Ile	Glu	Pro	Glu	Val	Leu	
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Tyr	Ala	Gly	Tyr	Asp	Ser	Ser	Val	Pro	Asp	Ser	Thr	Trp	Arg	Ile	Met	
545					550				555						560	
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Thr	Thr	Leu	Asn	Met	Leu	Gly	Gly	Arg	Gln	Val	Ile	Ala	Ala	Val	Lys	
			565						570					575		
tgg	gca	aag	gca	ata	cca	ggt	ttc	agg	aac	tta	cac	ctg	gat	gac	caa	1776
Trp	Ala	Lys	Ala	Ile	Pro	Gly	Phe	Arg	Asn	Leu	His	Leu	Asp	Asp	Gln	
		580						585					590			
atg	acc	cta	ctg	cag	tac	tcc	tgg	atg	gac	ctt	atg	gca	ttt	gct	ctg	1824
Met	Thr	Leu	Leu	Gln	Tyr	Ser	Trp	Met	Asp	Leu	Met	Ala	Phe	Ala	Leu	
		595					600					605				
ggg	tgg	aga	tca	tat	aga	caa	tca	agt	gca	aac	ctg	ctg	tgt	ttt	gct	1872
Gly	Trp	Arg	Ser	Tyr	Arg	Gln	Ser	Ser	Ala	Asn	Leu	Leu	Cys	Phe	Ala	
	610					615					620					
cct	gat	ctg	att	att	aat	gag	cag	aga	atg	act	cta	ccc	tgc	atg	tac	1920
Pro	Asp	Leu	Ile	Ile	Asn	Glu	Gln	Arg	Met	Thr	Leu	Pro	Cys	Met	Tyr	
625					630					635					640	
gac	caa	tgt	aaa	cac	atg	ctg	tat	gtt	tcc	tct	gag	tta	cac	agg	ctt	1968
Asp	Gln	Cys	Lys	His	Met	Leu	Tyr	Val	Ser	Ser	Glu	Leu	His	Arg	Leu	
				645					650					655		
cag	gta	tct	tat	gaa	gag	tat	ctc	tgt	atg	aaa	acc	tta	ctg	ctt	ctc	2016
Gln	Val	Ser	Tyr	Glu	Glu	Tyr	Leu	Cys	Met	Lys	Thr	Leu	Leu	Leu	Leu	
			660					665					670			
tct	tca	gtt	cct	aag	gac	ggt	ctg	aag	agc	caa	gag	cta	ttt	gat	gaa	2064
Ser	Ser	Val	Pro	Lys	Asp	Gly	Leu	Lys	Ser	Gln	Glu	Leu	Phe	Asp	Glu	
		675					680					685				
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Ile	Arg	Met	Thr	Tyr	Ile	Lys	Glu	Leu	Gly	Lys	Ala	Ile	Val	Lys	Arg	
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gaa	gga	aac	tcc	agc	cag	aac	tgg	cag	cgg	ttt	tat	caa	ctg	aca	aaa	2160
Glu	Gly	Asn	Ser	Ser	Gln	Asn	Trp	Gln	Arg	Phe	Tyr	Gln	Leu	Thr	Lys	
705					710					715					720	
ctc	ttg	gat	tct	atg	cat	gaa	gtg	gtt	gaa	aat	ctc	ctt	aac	tat	tgc	2208
Leu	Leu	Asp	Ser	Met	His	Glu	Val	Val	Glu	Asn	Leu	Leu	Asn	Tyr	Cys	
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ttc	caa	aca	ttt	ttg	gat	aag	acc	atg	agt	att	gaa	ttc	ccc	gag	atg	2256
Phe	Gln	Thr	Phe	Leu	Asp	Lys	Thr	Met	Ser	Ile	Glu	Phe	Pro	Glu	Met	
			740					745					750			
tta	gct	gaa	atc	atc	acc	aat	cag	ata	cca	aaa	tat	tca	aat	gga	aat	2304
Leu	Ala	Glu	Ile	Ile	Thr	Asn	Gln	Ile	Pro	Lys	Tyr	Ser	Asn	Gly	Asn	
		755					760					765				
atc	aaa	aaa	ctt	ctg	ttt	cat	caa	aag	tga							2334
Ile	Lys	Lys	Leu	Leu	Phe	His	Gln	Lys								
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<211> 777

<212> PRT

<213> Homo sapiens

<400> 6

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 Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu
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 Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp
 50 55 60
 Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys
 65 70 75 80
 Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys
 85 90 95
 Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu
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 Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn
 115 120 125
 Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser
 130 135 140
 Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His
 145 150 155 160
 Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr
 165 170 175
 Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp
 180 185 190
 Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr
 195 200 205
 Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu
 210 215 220
 Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn
 225 230 235 240
 Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys
 245 250 255
 Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr
 260 265 270
 Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr
 275 280 285
 Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala
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Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser
 305 310 315 320
 Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met
 325 330 335
 Asn Thr Ala Ser Leu Ser Gln Gln Gln Asp Gln Lys Pro Ile Phe Asn
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 Val Ile Pro Pro Ile Pro Val Gly Ser Glu Asn Trp Asn Arg Cys Gln
 355 360 365
 Gly Ser Gly Asp Asp Asn Leu Thr Ser Leu Gly Thr Leu Asn Phe Pro
 370 375 380
 Gly Arg Thr Val Phe Ser Asn Gly Tyr Ser Ser Pro Ser Met Arg Pro
 385 390 395 400
 Asp Val Ser Ser Pro Pro Ser Ser Ser Ser Thr Ala Thr Thr Gly Pro
 405 410 415
 Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His
 420 425 430
 Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala
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 Val Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp Cys Ile
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 Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Tyr Arg Lys
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 Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys Lys Lys
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 Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr Ser
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 Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Leu Pro Gln Leu
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 Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile Met
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 Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys
 565 570 575
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 580 585 590
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 595 600 605

Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala
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Pro Asp Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Cys Met Tyr
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Asp Gln Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu
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Gln Val Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu
 660 665 670

Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu
 675 680 685

Ile Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg
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Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys
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Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys
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Phe Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met
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<210> 7

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<212> DNA

<213> Homo sapiens

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<222> (1)..(2334)

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<223> n = a or c or g or t/u

<400> 7

19/57

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cta aga gga gga gct act gtg aag gtt tct gcg tct tca ccc tca ctg Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu 35 40 45	144
gct gtc gct tct caa tca gac tcc aag cag cga aga ctt ttg gtt gat Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp 50 55 60	192
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gca gtt tca ctc tca atg gga ctg tat atg gga gag aca gaa aca aaa Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys 85 90 95	288
gtg atg gga aat gac ctg gga ttc cca cag cag ggc caa atc agc ctt Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu 100 105 110	336
tcc tcg ggg gaa aca gac tta aag ctt ttg gaa gaa agc att gca aac Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn 115 120 125	384
ctc aat agg tcg acc agt gtt cca gag aac ccc aag agt tca gca tcc Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser 130 135 140	432
act gct gtg tct gct gcc ccc aca gag aag gag ttt cca aaa act cac Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His 145 150 155 160	480
tct gat gta tct tca gaa cag caa cat ttg aag ggc cag act ggc acc Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr 165 170 175	528
aac ggt ggc aat gtg aaa ttg tat acc aca gac caa agc acc ttt gac Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp 180 185 190	576
att ttg cag gat ttg gag ttt tct tct ggg tcc cca ggt aaa gag acg Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr 195 200 205	624
aat gag agt cct tgg aga tca gac ctg ttg ata gat gaa aac tgt ttg Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu 210 215 220	672
ctt tct cct ctg gcg gga gaa gac gat tca ttc ctt ttg gaa gga aac Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn 225 230 235 240	720
tcg aat gag gac tgc aag cct ctc att tta ccg gac act aaa ccc aaa Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys 245 250 255	768
att aag gat aat gga gat ctg gtt ttg tca agc ccc agt aat gta aca Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr 260 265 270	816
ctg ccc caa gtg aaa aca gaa aaa gaa gat ttc atc gaa ctc tgc acc Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr 275 280 285	864
cct ggg gta att aag caa gag aaa ctg ggc aca gtt tac tgt cag gca Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala 290 295 300	912

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gtt cat ggt gtg agt acc tct gga gga cag atg tac cac tat gac atg Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met 325 330 335	1008
aat aca gca tcc ctt tct caa cag cag gat cag aag cct att ttt aat Asn Thr Ala Ser Leu Ser Gln Gln Gln Asp Gln Lys Pro Ile Phe Asn 340 345 350	1056
gtc att cca cca att ccc gtt ggt tcc gaa aat tgg aat agg tgc caa Val Ile Pro Pro Ile Pro Val Gly Ser Glu Asn Trp Asn Arg Cys Gln 355 360 365	1104
gga tct gga gat gac aac ttg act tct ctg ggg act ctg aac ttc cct Gly Ser Gly Asp Asp Asn Leu Thr Ser Leu Gly Thr Leu Asn Phe Pro 370 375 380	1152
ggc cga aca gtt ttt tct aat ggc tat tca agc ccc agc atg aga cca Gly Arg Thr Val Phe Ser Asn Gly Tyr Ser Ser Pro Ser Met Arg Pro 385 390 395 400	1200
gat gta agc tct cct cca tcc agc tcc tca aca gca aca aca gga cca Asp Val Ser Ser Pro Pro Ser Ser Ser Thr Ala Thr Thr Gly Pro 405 410 415	1248
cct ccc aaa ctc tgc ctg gtg tgc tct gat gaa gct tca gga tgt cat Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His 420 425 430	1296
tat gga gtc tta act tgt gga agc tgt aaa gtt ttc ttc aaa aga gca Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala 435 440 445	1344
gtg gaa gga cag cac aat tac cta tgt gct gga agg aat gat tgc atc Val Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp Cys Ile 450 455 460	1392
atc gat aaa att cga aga aaa aac tgc cca gca tgc cgc tat cga aaa Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Tyr Arg Lys 465 470 475 480	1440
tgt ctt cag gct gga atg aac ctg gaa gct cga aaa aca aag aaa aaa Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys Lys Lys 485 490 495	1488
ata aaa gga att cag cag gcc act aca gga gtc tca caa gaa acc tct Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr Ser 500 505 510	1536
gaa aat cct ggt aac aaa aca ata gtt cct gca acg tta cca caa ctc Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Leu Pro Gln Leu 515 520 525	1584
acc cct acc ctg gtg tca nnn ttg gag nnn att gaa cct gaa gtg tta Thr Pro Thr Leu Val Ser Xaa Leu Glu Xaa Ile Glu Pro Glu Val Leu 530 535 540	1632
tat gca gga tat gat agc tct nnn cca gac tca act nnn agg atc atg Tyr Ala Gly Tyr Asp Ser Ser Xaa Pro Asp Ser Thr Xaa Arg Ile Met 545 550 555 560	1680
act acg ctc aac atg tta gga ggg cgg caa gtg att gca gca gtg aaa Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys 565 570 575	1728
tgg gca aag gca ata cca ggt ttc agg aac tta cac ctg gat gac caa Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln 580 585 590	1776
atg acc cta ctg cag tac tcc tgg atg nnn ctt atg gca ttt gct ctg Met Thr Leu Leu Gln Tyr Ser Trp Met Xaa Leu Met Ala Phe Ala Leu 595 600 605	1824

ggg tgg aga tca tat aga caa tca agt gca aac ctg ctg tgt ttt gct 1872
 Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala
 610 615 620

cct gat ctg att att aat gag cag aga atg act nnn ccc nnn atg tac 1920
 Pro Asp Leu Ile Ile Asn Glu Gln Arg Met Thr Xaa Pro Xaa Met Tyr
 625 630 635 640

gac caa tgt aaa cac atg ctg nnn gtt tcc tct gag tta cac agg ctt 1968
 Asp Gln Cys Lys His Met Leu Xaa Val Ser Ser Glu Leu His Arg Leu
 645 650 655

cag gta tct nnn gaa gag tat ctc tgt atg aaa acc tta ctg ctt ctc 2016
 Gln Val Ser Xaa Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu
 660 665 670

tct tca gtt cct aag gac ggt ctg aag agc caa gag nnn ttt gat gaa 2064
 Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Xaa Phe Asp Glu
 675 680 685

att aga nnn acc tac atc aaa gag cta gga aaa gcc att nnn aag agg 2112
 Ile Arg Xaa Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Xaa Lys Arg
 690 695 700

gaa gga aac tcc agc cag aac nnn cag cgg ttt tat caa ctg aca aaa 2160
 Glu Gly Asn Ser Ser Gln Asn Xaa Gln Arg Phe Tyr Gln Leu Thr Lys
 705 710 715 720

ctc ttg gat tct atg cat gaa gtg gtt gaa aat ctc nnn aac tat tgc 2208
 Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Xaa Asn Tyr Cys
 725 730 735

ttc caa aca ttt nnn gat aag acc atg agt att gaa ttc ccc gag atg 2256
 Phe Gln Thr Phe Xaa Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met
 740 745 750

tta gct gaa atc atc acc aat cag ata cca aaa nnn tca aat gga aat 2304
 Leu Ala Glu Ile Ile Thr Asn Gln Ile Pro Lys Xaa Ser Asn Gly Asn
 755 760 765

atc aaa aaa ctt ctg ttt cat caa aag tga 2334
 Ile Lys Lys Leu Leu Phe His Gln Lys
 770 775

<210> 8

<211> 777

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<222> (535)..(535)

<223> The 'Xaa' at location 535 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (538)..(538)

<223> The 'Xaa' at location 538 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (552)..(552)

<223> The 'Xaa' at location 552 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (557)..(557)

<223> The 'Xaa' at location 557 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (602)..(602)

<223> The 'Xaa' at location 602 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (636)..(636)

<223> The 'Xaa' at location 636 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (638)..(638)

<223> The 'Xaa' at location 638 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (648)..(648)

<223> The 'Xaa' at location 648 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (660)..(660)

<223> The 'Xaa' at location 660 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (685)..(685)

<223> The 'Xaa' at location 685 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (691)..(691)

<223> The 'Xaa' at location 691 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (702)..(702)

<223> The 'Xaa' at location 702 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (712)..(712)

<223> The 'Xaa' at location 712 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (733)..(733)

<223> The 'Xaa' at location 733 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (741)..(741)

<223> The 'Xaa' at location 741 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (764)..(764)

<223> The 'Xaa' at location 764 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (1)..(2334)

<223> n = a or c or g or t/u

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Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr
 20 25 30
 Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu
 35 40 45
 Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp
 50 55 60
 Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys
 65 70 75 80
 Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys
 85 90 95
 Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu
 100 105 110
 Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn
 115 120 125
 Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser
 130 135 140
 Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His
 145 150 155 160
 Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr
 165 170 175
 Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp
 180 185 190
 Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr
 195 200 205
 Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu
 210 215 220
 Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn
 225 230 235 240
 Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys
 245 250 255
 Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr
 260 265 270
 Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr
 275 280 285
 Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala
 290 295 300
 Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser

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305 310 315 320
 Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met
 325 330 335
 Asn Thr Ala Ser Leu Ser Gln Gln Gln Asp Gln Lys Pro Ile Phe Asn
 340 345 350
 Val Ile Pro Pro Ile Pro Val Gly Ser Glu Asn Trp Asn Arg Cys Gln
 355 360 365
 Gly Ser Gly Asp Asp Asn Leu Thr Ser Leu Gly Thr Leu Asn Phe Pro
 370 375 380
 Gly Arg Thr Val Phe Ser Asn Gly Tyr Ser Ser Pro Ser Met Arg Pro
 385 390 395 400
 Asp Val Ser Ser Pro Pro Ser Ser Ser Ser Thr Ala Thr Thr Gly Pro
 405 410 415
 Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His
 420 425 430
 Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala
 435 440 445
 Val Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp Cys Ile
 450 455 460
 Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Tyr Arg Lys
 465 470 475 480
 Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys Lys Lys
 485 490 495
 Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr Ser
 500 505 510
 Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Leu Pro Gln Leu
 515 520 525
 Thr Pro Thr Leu Val Ser Xaa Leu Glu Xaa Ile Glu Pro Glu Val Leu
 530 535 540
 Tyr Ala Gly Tyr Asp Ser Ser Xaa Pro Asp Ser Thr Xaa Arg Ile Met
 545 550 555 560
 Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys
 565 570 575
 Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln
 580 585 590
 Met Thr Leu Leu Gln Tyr Ser Trp Met Xaa Leu Met Ala Phe Ala Leu
 595 600 605
 Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala

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610 615 620
 Pro Asp Leu Ile Ile Asn Glu Gln Arg Met Thr Xaa Pro Xaa Met Tyr
 625 630 635 640
 Asp Gln Cys Lys His Met Leu Xaa Val Ser Ser Glu Leu His Arg Leu
 645 650 655
 Gln Val Ser Xaa Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu
 660 665 670
 Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Xaa Phe Asp Glu
 675 680 685
 Ile Arg Xaa Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Xaa Lys Arg
 690 695 700
 Glu Gly Asn Ser Ser Gln Asn Xaa Gln Arg Phe Tyr Gln Leu Thr Lys
 705 710 715 720
 Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Xaa Asn Tyr Cys
 725 730 735
 Phe Gln Thr Phe Xaa Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met
 740 745 750
 Leu Ala Glu Ile Ile Thr Asn Gln Ile Pro Lys Xaa Ser Asn Gly Asn
 755 760 765
 Ile Lys Lys Leu Leu Phe His Gln Lys
 770 775

<210> 9

<211> 774

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(774)

<223>

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 1 5 10 15
 gag gtt att gaa cct gaa gtg tta tat gca gga tat gat agc tct gtt 96
 Glu Val Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Val
 20 25 30
 cca gac tca act tgg agg atc atg act acg ctc aac atg tta gga ggg 144
 Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
 35 40 45

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cgg caa gtg att gca gca gtg aaa tgg gca aag gca ata cca ggt ttc 192
 Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
 50 55 60

agg aac tta cac ctg gat gac caa atg acc cta ctg cag tac tcc tgg 240
 Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
 65 70 75 80

atg ttt ctt atg gca ttt gct ctg ggg tgg aga tca tat aga caa tca 288
 Met Phe Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
 85 90 95

agt gca aac ctg ctg tgt ttt gct cct gat ctg att att aat gag cag 336
 Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
 100 105 110

aga atg act cta ccc tgc atg tac gac caa tgt aaa cac atg ctg tat 384
 Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
 115 120 125

gtt tcc tct gag tta cac agg ctt cag gta tct tat gaa gag tat ctc 432
 Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
 130 135 140

tgt atg aaa acc tta ctg ctt ctc tct tca gtt cct aag gac ggt ctg 480
 Cys Met Lys Thr Leu Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
 145 150 155 160

aag agc caa gag cta ttt gat gaa att aga atg acc tac atc aaa gag 528
 Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
 165 170 175

cta gga aaa gcc att gtc aag agg gaa gga aac tcc agc cag aac tgg 576
 Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
 180 185 190

cag cgg ttt tat caa ctg aca aaa ctc ttg gat tct atg cat gaa gtg 624
 Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
 195 200 205

gtt gaa aat ctc ctt aac tat tgc ttc caa aca ttt ttg gat aag acc 672
 Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
 210 215 220

atg agt att gaa ttc ccc gag atg tta gct gaa atc atc acc aat cag 720
 Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
 225 230 235 240

ata cca aaa tat tca aat gga aat atc aaa aaa ctt ctg ttt cat caa 768
 Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
 245 250 255

aag tga 774
 Lys

<210> 10

<211> 257

<212> PRT

<213> Homo sapiens

<400> 10

Val Pro Ala Thr Leu Pro Gln Leu Thr Pro Thr Leu Val Ser Leu Leu
 1 5 10 15

Glu Val Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Val
 20 25 30

Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
 35 40 45
 Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
 50 55 60
 Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
 65 70 75 80
 Met Phe Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
 85 90 95
 Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
 100 105 110
 Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
 115 120 125
 Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
 130 135 140
 Cys Met Lys Thr Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
 145 150 155 160
 Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
 165 170 175
 Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
 180 185 190
 Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
 195 200 205
 Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
 210 215 220
 Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
 225 230 235 240
 Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
 245 250 255

Lys

<210> 11

<211> 1548

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

29/57

<222> (1)..(774)

<223>

<400> 11

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gtt cct gca acg tta cca caa ctc acc cct acc ctg gtg tca ctg ttg      48
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1          5          10          15

gag gtt att gaa cct gaa gtg tta tat gca gga tat gat agc tct gtt      96
Glu Val Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Val
20          25          30

cca gac tca act tgg agg atc atg act acg ctc aac atg tta gga ggg      144
Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
35          40          45

cgg caa gtg att gca gca gtg aaa tgg gca aag gca ata cca ggt ttc      192
Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
50          55          60

agg aac tta cac ctg gat gac caa atg acc cta ctg cag tac tcc tgg      240
Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
65          70          75          80

atg tcc ctt atg gca ttt gct ctg ggg tgg aga tca tat aga caa tca      288
Met Ser Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
85          90          95

agt gca aac ctg ctg tgt ttt gct cct gat ctg att att aat gag cag      336
Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
100         105         110

aga atg act cta ccc tgc atg tac gac caa tgt aaa cac atg ctg tat      384
Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
115         120         125

gtt tcc tct gag tta cac agg ctt cag gta tct tat gaa gag tat ctc      432
Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
130         135         140

tgt atg aaa acc tta ctg ctt ctc tct tca gtt cct aag gac ggt ctg      480
Cys Met Lys Thr Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
145         150         155         160

aag agc caa gag cta ttt gat gaa att aga atg acc tac atc aaa gag      528
Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
165         170         175

cta gga aaa gcc att gtc aag agg gaa gga aac tcc agc cag aac tgg      576
Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
180         185         190

cag cgg ttt tat caa ctg aca aaa ctc ttg gat tct atg cat gaa gtg      624
Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
195         200         205

gtt gaa aat ctc ctt aac tat tgc ttc caa aca ttt ttg gat aag acc      672
Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
210         215         220

atg agt att gaa ttc ccc gag atg tta gct gaa atc atc acc aat cag      720
Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
225         230         235         240

ata cca aaa tat tca aat gga aat atc aaa aaa ctt ctg ttt cat caa      768
Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
245         250         255

aag tga gttcctgcaa cggtaccaca actcaccct accctggtgt cactgttgga      824
Lys

ggttattgaa cctgaagtgt tatatgcagg atatgatagc tctgttccag actcaacttg      884

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gaggatcatg actacgctca acatgttagg agggcggcaa gtgattgcag cagtgaaatg 944
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 gtga 1548

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<211> 257

<212> PRT

<213> Homo sapiens

<400> 12

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 20 25 30
 Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
 35 40 45
 Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
 50 55 60
 Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
 65 70 75 80
 Met Ser Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
 85 90 95
 Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
 100 105 110
 Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
 115 120 125
 Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
 130 135 140
 Cys Met Lys Thr Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
 145 150 155 160

Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
 165 170 175

Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
 180 185 190

Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
 195 200 205

Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
 210 215 220

Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
 225 230 235 240

Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
 245 250 255

Lys

<210> 13

<211> 774

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(774)

<223>

<400> 13

gtt cct gca acg tta cca caa ctc acc cct acc ctg gtg tca ctg ttg 48
 Val Pro Ala Thr Leu Pro Gln Leu Thr Pro Thr Leu Val Ser Leu Leu
 1 5 10 15

gag gtt att gaa cct gaa gtg tta tat gca gga tat gat agc tct gtt 96
 Glu Val Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Val
 20 25 30

cca gac tca act tgg agg atc atg act acg ctc aac atg tta gga ggg 144
 Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
 35 40 45

cgg caa gtg att gca gca gtg aaa tgg gca aag gca ata cca ggt ttc 192
 Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
 50 55 60

agg aac tta cac ctg gat gac caa atg acc cta ctg cag tac tcc tgg 240
 Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
 65 70 75 80

atg gac ctt atg gca ttt gct ctg ggg tgg aga tca tat aga caa tca 288
 Met Asp Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
 85 90 95

agt gca aac ctg ctg tgt ttt gct cct gat ctg att att aat gag cag 336
 Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
 100 105 110
 aga atg act cta ccc tgc atg tac gac caa tgt aaa cac atg ctg tat 384
 Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
 115 120 125
 gtt tcc tct gag tta cac agg ctt cag gta tct tat gaa gag tat ctc 432
 Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
 130 135 140
 tgt atg aaa acc tta ctg ctt ctc tct tca gtt cct aag gac ggt ctg 480
 Cys Met Lys Thr Leu Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
 145 150 155 160
 aag agc caa gag cta ttt gat gaa att aga atg acc tac atc aaa gag 528
 Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
 165 170 175
 cta gga aaa gcc att gtc aag agg gaa gga aac tcc agc cag aac tgg 576
 Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
 180 185 190
 cag cgg ttt tat caa ctg aca aaa ctc ttg gat tct atg cat gaa gtg 624
 Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
 195 200 205
 gtt gaa aat ctc ctt aac tat tgc ttc caa aca ttt ttg gat aag acc 672
 Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
 210 215 220
 atg agt att gaa ttc ccc gag atg tta gct gaa atc atc acc aat cag 720
 Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
 225 230 235 240
 ata cca aaa tat tca aat gga aat atc aaa aaa ctt ctg ttt cat caa 768
 Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
 245 250 255
 aag tga
 Lys 774

<210> 14

<211> 257

<212> PRT

<213> Homo sapiens

<400> 14

Val Pro Ala Thr Leu Pro Gln Leu Thr Pro Thr Leu Val Ser Leu Leu
 1 5 10 15
 Glu Val Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Val
 20 25 30
 Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
 35 40 45
 Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
 50 55 60
 Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
 65 70 75 80

Met Asp Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
85 90 95

Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
100 105 110

Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
115 120 125

Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
130 135 140

Cys Met Lys Thr Leu Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
145 150 155 160

Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
165 170 175

Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
180 185 190

Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
195 200 205

Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
210 215 220

Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
225 230 235 240

Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
245 250 255

Lys

<210> 15

<211> 774

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(774)

<223> n = a or c or g or t/u such that Xaa at positions 552, 557, 602, 636, 648, 712, 741, 535, 538, 638, 691, 702, 648, 660, 685, 733 and 764 can independently be Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (1)..(774)

<223> n = a or c or g or t/u such that Xaa at positions 552, 557, 602, 636, 648, 712, 741, 535, 538, 638, 691, 702, 648, 660, 685, 733 and 764 can independently be Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr

<400> 15
 gtt cct gca acg tta cca caa ctc acc cct acc ctg gtg tca nnn ttg 48
 Val Pro Ala Thr Leu Pro Gln Leu Thr Pro Thr Leu Val Ser Xaa Leu
 1 5 10 15
 gag nnn att gaa cct gaa gtg tta tat gca gga tat gat agc tct nnn 96
 Glu Xaa Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Xaa
 20 25 30
 cca gac tca act nnn agg atc atg act acg ctc aac atg tta gga ggg 144
 Pro Asp Ser Thr Xaa Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
 35 40 45
 cgg caa gtg att gca gca gtg aaa tgg gca aag gca ata cca ggt ttc 192
 Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
 50 55 60
 agg aac tta cac ctg gat gac caa atg acc cta ctg cag tac tcc tgg 240
 Arg Asn Leu His Leu Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
 65 70 75 80
 atg nnn ctt atg gca ttt gct ctg ggg tgg aga tca tat aga caa tca 288
 Met Xaa Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
 85 90 95
 agt gca aac ctg ctg tgt ttt gct cct gat ctg att att aat gag cag 336
 Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
 100 105 110
 aga atg act nnn ccc nnn atg tac gac caa tgt aaa cac atg ctg nnn 384
 Arg Met Thr Xaa Pro Xaa Met Tyr Asp Gln Cys Lys His Met Leu Xaa
 115 120 125
 gtt tcc tct gag tta cac agg ctt cag gta tct nnn gaa gag tat ctc 432
 Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Xaa Glu Glu Tyr Leu
 130 135 140
 tgt atg aaa acc tta ctg ctt ctc tct tca gtt cct aag gac ggt ctg 480
 Cys Met Lys Thr Leu Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
 145 150 155 160
 aag agc caa gag nnn ttt gat gaa att aga nnn acc tac atc aaa gag 528
 Lys Ser Gln Glu Xaa Phe Asp Glu Ile Arg Xaa Thr Tyr Ile Lys Glu
 165 170 175
 cta gga aaa gcc att nnn aag agg gaa gga aac tcc agc cag aac nnn 576
 Leu Gly Lys Ala Ile Xaa Lys Arg Glu Gly Asn Ser Ser Gln Asn Xaa
 180 185 190
 cag cgg ttt tat caa ctg aca aaa ctc ttg gat tct atg cat gaa gtg 624
 Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
 195 200 205
 gtt gaa aat ctc nnn aac tat tgc ttc caa aca ttt nnn gat aag acc 672
 Val Glu Asn Leu Xaa Asn Tyr Cys Phe Gln Thr Phe Xaa Asp Lys Thr
 210 215 220
 atg agt att gaa ttc ccc gag atg tta gct gaa atc atc acc aat cag 720
 Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
 225 230 235 240
 ata cca aaa nnn tca aat gga aat atc aaa aaa ctt ctg ttt cat caa 768
 Ile Pro Lys Xaa Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
 245 250 255

aag tga
Lys

774

<210> 16

<211> 257

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<222> (15)..(15)

<223> The 'Xaa' at location 15 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (18)..(18)

<223> The 'Xaa' at location 18 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (32)..(32)

<223> The 'Xaa' at location 32 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (37)..(37)

<223> The 'Xaa' at location 37 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (82)..(82)

<223> The 'Xaa' at location 82 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (116)..(116)

<223> The 'Xaa' at location 116 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (118)..(118)

<223> The 'Xaa' at location 118 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (128)..(128)

<223> The 'Xaa' at location 128 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (140)..(140)

<223> The 'Xaa' at location 140 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (165)..(165)

<223> The 'Xaa' at location 165 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (171)..(171)

<223> The 'Xaa' at location 171 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (182)..(182)

<223> The 'Xaa' at location 182 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (192)..(192)

<223> The 'Xaa' at location 192 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (213)..(213)

<223> The 'Xaa' at location 213 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (221)..(221)

<223> The 'Xaa' at location 221 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (244)..(244)

<223> The 'Xaa' at location 244 stands for Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr.

<220>

<221> misc_feature

<222> (1)..(774)

<223> n = a or c or g or t/u such that Xaa at positions 552, 557, 602, 636, 648, 712, 741, 535, 538, 638, 691, 702, 648, 660, 685, 733 and 764 can independently be Cys, Asn, Tyr, Lys, Ser, Asp, Glu, Gln, Arg or Thr

<400> 16

Val Pro Ala Thr Leu Pro Gln Leu Thr Pro Thr Leu Val Ser Xaa Leu
1 5 10 15

Glu Xaa Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Xaa
20 25 30

Pro Asp Ser Thr Xaa Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
35 40 45

Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
50 55 60

Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
65 70 75 80

Met Xaa Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
85 90 95

Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
100 105 110

Arg Met Thr Xaa Pro Xaa Met Tyr Asp Gln Cys Lys His Met Leu Xaa
115 120 125

Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Xaa Glu Glu Tyr Leu
130 135 140

Cys Met Lys Thr Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
145 150 155 160

Lys Ser Gln Glu Xaa Phe Asp Glu Ile Arg Xaa Thr Tyr Ile Lys Glu
 165 170 175

Leu Gly Lys Ala Ile Xaa Lys Arg Glu Gly Asn Ser Ser Gln Asn Xaa
 180 185 190

Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
 195 200 205

Val Glu Asn Leu Xaa Asn Tyr Cys Phe Gln Thr Phe Xaa Asp Lys Thr
 210 215 220

Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
 225 230 235 240

Ile Pro Lys Xaa Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
 245 250 255

Lys

<210> 17

<211> 25

<212> PRT

<213> Homo sapiens

<400> 17

Gln Glu Pro Val Ser Pro Lys Lys Lys Glu Asn Ala Leu Leu Arg Tyr
 1 5 10 15

Leu Leu Asp Lys Asp Asp Thr Lys Asp
 20 25

<210> 18

<211> 5

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)..(5)

<223> Xaa is any amino acid

<400> 18

Leu Xaa Xaa Leu Leu
 1 5

<210> 19

<211> 67

<212> DNA

<213> Homo sapiens

<400> 19

cggcggcgcc atatgaaaaa aggtcatcat catcatcatc atgggtcccc tatactaggt 60
tattgga 67

<210> 20

<211> 33

<212> DNA

<213> Homo sapiens

<400> 20

cggcggcgcg gatccacgcg gaaccagatc cga 33

<210> 21

<211> 237

<212> PRT

<213> Homo sapiens

<400> 21

Met Lys Lys Gly His His His His His His His Gly Ser Pro Ile Leu
1 5 10 15

Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro Thr Arg Leu Leu Leu
20 25 30

Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu Tyr Glu Arg Asp Glu
35 40 45

Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu Gly Leu Glu Phe Pro
50 55 60

Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys Leu Thr Gln Ser Met
65 70 75 80

Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn Met Leu Gly Gly Cys
85 90 95

Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu Gly Ala Val Leu Asp
100 105 110

Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser Lys Asp Phe Glu Thr
115 120 125

Leu Lys Val Asp Phe Leu Ser Lys Leu Pro Glu Met Leu Lys Met Phe
130 135 140

Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn Gly Asp His Val Thr
145 150 155 160

His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp Val Val Leu Tyr Met
165 170 175

Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu Val Cys Phe Lys Lys
180 185 190

Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr Leu Lys Ser Ser Lys
195 200 205

Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala Thr Phe Gly Gly Gly
210 215 220

Asp His Pro Pro Lys Ser Asp Leu Val Pro Arg Gly Ser
225 230 235

<210> 22

<211> 32

<212> DNA

<213> Homo sapiens

<400> 22
tactcctgga tgtcccttat ggcatttgct ct

32

<210> 23

<211> 32

<212> DNA

<213> Homo sapiens

<400> 23
agagcaaagc ccataaggga catccaggag ta

32

<210> 24

<211> 32

<212> DNA

<213> Homo sapiens

<400> 24
tactcctgga tggaccttat ggcatttgct ct

32

<210> 25

<211> 32

<212> DNA

<213> Homo sapiens

<400> 25
agagcaaatg ccataaggtc catccaggag ta

32

<210> 26

<211> 252

<212> PRT

<213> Homo sapiens

<400> 26

Ala Leu Thr Pro Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu
1 5 10 15

Ile Val Tyr Ala Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn
20 25 30

Leu Leu Ser Thr Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val
35 40 45

Val Lys Trp Ala Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu
50 55 60

Asp Gln Ile Thr Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe
65 70 75 80

Ala Leu Ser Trp Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr
85 90 95

Phe Ala Pro Asp Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala
100 105 110

Met Tyr Glu Leu Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val
115 120 125

Arg Leu Gln Leu Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu
130 135 140

Leu Leu Ser Thr Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe
145 150 155 160

Glu Glu Met Arg Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr
165 170 175

Lys Cys Pro Asn Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu
180 185 190

Thr Lys Leu Leu Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu
195 200 205

Phe Cys Phe Tyr Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe
210 215 220

Pro Ala Met Leu Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu
225 230 235 240

Ser Gly Asn Ala Lys Pro Leu Tyr Phe His Arg Lys
 245 250

<210> 27

<211> 252

<212> PRT

<213> Homo sapiens

<400> 27

Gln Leu Ile Pro Pro Leu Ile Asn Leu Leu Met Ser Ile Glu Pro Asp
 1 5 10 15

Val Ile Tyr Ala Gly His Asp Asn Thr Lys Pro Asp Thr Ser Ser Ser
 20 25 30

Leu Leu Thr Ser Leu Asn Gln Leu Gly Glu Arg Gln Leu Leu Ser Val
 35 40 45

Val Lys Trp Ser Lys Ser Leu Pro Gly Phe Arg Asn Leu His Ile Asp
 50 55 60

Asp Gln Ile Thr Leu Ile Gln Tyr Ser Trp Met Ser Leu Met Val Phe
 65 70 75 80

Gly Leu Gly Trp Arg Ser Tyr Lys His Val Ser Gly Gln Met Leu Tyr
 85 90 95

Phe Ala Pro Asp Leu Ile Leu Asn Glu Gln Arg Met Lys Glu Ser Ser
 100 105 110

Phe Tyr Ser Leu Cys Leu Thr Met Trp Gln Ile Pro Gln Glu Phe Val
 115 120 125

Lys Leu Gln Val Ser Gln Glu Glu Phe Leu Cys Met Lys Val Leu Leu
 130 135 140

Leu Leu Asn Thr Ile Pro Leu Glu Gly Leu Arg Ser Gln Thr Gln Phe
 145 150 155 160

Glu Glu Met Arg Ser Ser Tyr Ile Arg Glu Leu Ile Lys Ala Ile Gly
 165 170 175

Leu Arg Gln Lys Gly Val Val Ser Ser Ser Gln Arg Phe Tyr Gln Leu
 180 185 190

Thr Lys Leu Leu Asp Asn Leu His Asp Leu Val Lys Gln Leu His Leu
 195 200 205

Tyr Cys Leu Asn Thr Phe Ile Gln Ser Arg Ala Leu Ser Val Glu Phe
 210 215 220

Pro Glu Met Met Ser Glu Val Ile Ala Ala Gln Leu Pro Lys Ile Leu
 225 230 235 240

Ala Gly Met Val Lys Pro Leu Leu Phe His Lys Lys
 245 250

<210> 28

<211> 252

<212> PRT

<213> Homo sapiens

<400> 28

Glu Cys Gln Pro Ile Phe Leu Asn Val Leu Glu Ala Ile Glu Pro Gly
 1 5 10 15

Val Val Cys Ala Gly His Asp Asn Asn Gln Pro Asp Ser Phe Ala Ala
 20 25 30

Leu Leu Ser Ser Leu Asn Glu Leu Gly Glu Arg Gln Leu Val His Val
 35 40 45

Val Lys Trp Ala Lys Ala Leu Pro Gly Phe Arg Asn Leu His Val Asp
 50 55 60

Asp Gln Met Ala Val Ile Gln Tyr Ser Trp Met Gly Leu Met Val Phe
 65 70 75 80

Ala Met Gly Trp Arg Ser Phe Thr Asn Val Asn Ser Arg Met Leu Tyr
 85 90 95

Phe Ala Pro Asp Leu Val Phe Asn Glu Tyr Arg Met His Lys Ser Arg
 100 105 110

Met Tyr Ser Gln Cys Val Arg Met Arg His Leu Ser Gln Glu Phe Gly
 115 120 125

Trp Leu Gln Ile Thr Pro Gln Glu Phe Leu Cys Met Lys Ala Leu Leu
 130 135 140

Leu Phe Ser Ile Ile Pro Val Asp Gly Leu Lys Asn Gln Lys Phe Phe
 145 150 155 160

Asp Glu Leu Arg Met Asn Tyr Ile Lys Glu Leu Asp Arg Ile Ile Ala
 165 170 175

Cys Lys Arg Lys Asn Pro Thr Ser Cys Ser Arg Arg Phe Tyr Gln Leu
 180 185 190

Thr Lys Leu Leu Asp Ser Val Gln Pro Ile Ala Arg Glu Leu His Gln
 195 200 205

Phe Thr Phe Asp Leu Leu Ile Lys Ser His Met Val Ser Val Asp Phe
 210 215 220

Pro Glu Met Met Ala Glu Ile Ile Ser Val Gln Val Pro Lys Ile Leu
 225 230 235 240

Ser Gly Lys Val Lys Pro Ile Tyr Phe His Thr Gln
 245 250

<210> 29

<211> 286

<212> PRT

<213> Homo sapiens

<400> 29

Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu Asp Ala Glu Pro Pro
 1 5 10 15

Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro Phe Ser Glu Ala Ser
 20 25 30

Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
 35 40 45

Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His
 50 55 60

Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile
 65 70 75 80

Gly Leu Val Trp Arg Ser Met Glu His Pro Gly Lys Leu Leu Phe Ala
 85 90 95

Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met
 100 105 110

Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser Ser Arg Phe Arg Met
 115 120 125

Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu
 130 135 140

Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr Leu Lys Ser Leu
 145 150 155 160

Glu Glu Lys Asp His Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr
 165 170 175

Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr Leu Gln Gln Gln His
 180 185 190

Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met
 195 200 205

Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val
 210 215 220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His Arg Leu
 225 230 235 240

His Ala Pro Thr Ser Arg Gly Gly Ala Ser Val Glu Glu Thr Asp Gln
245 250 255

Ser His Leu Ala Thr Ala Gly Ser Thr Ser Ser His Ser Leu Gln Lys
260 265 270

Tyr Tyr Ile Thr Gly Glu Ala Glu Gly Phe Pro Ala Thr Val
275 280 285

<210> 30

<211> 268

<212> PRT

<213> Homo sapiens

<400> 30

Leu Ser Pro Glu Gln Leu Val Leu Thr Leu Leu Glu Ala Glu Pro Pro
1 5 10 15

His Val Leu Ile Ser Arg Pro Ser Ala Pro Phe Thr Glu Ala Ser Met
20 25 30

Met Met Ser Leu Thr Lys Leu Ala Asp Lys Glu Leu Val His Met Ile
35 40 45

Ser Trp Ala Lys Lys Ile Pro Gly Phe Val Glu Leu Ser Leu Phe Asp
50 55 60

Gln Val Arg Leu Leu Glu Ser Cys Trp Met Glu Val Leu Met Met Gly
65 70 75 80

Leu Met Trp Arg Ser Ile Asp His Pro Gly Lys Leu Ile Phe Ala Pro
85 90 95

Asp Leu Val Leu Asp Arg Asp Glu Gly Lys Cys Val Glu Gly Ile Leu
100 105 110

Glu Ile Phe Asp Met Leu Leu Ala Thr Thr Ser Arg Phe Arg Glu Leu
115 120 125

Lys Leu Gln His Lys Glu Tyr Leu Cys Val Lys Ala Met Ile Leu Leu
130 135 140

Asn Ser Ser Met Tyr Pro Leu Val Thr Ala Thr Gln Asp Ala Asp Ser
145 150 155 160

Ser Arg Lys Leu Ala His Leu Leu Asn Ala Val Thr Asp Ala Leu Val
165 170 175

Trp Val Ile Ala Lys Ser Gly Ile Ser Ser Gln Gln Gln Ser Met Arg
180 185 190

Leu Ala Asn Leu Leu Met Leu Leu Ser His Val Arg His Ala Ser Asn

195

200

205

Lys Gly Met Glu His Leu Leu Asn Met Lys Cys Lys Asn Val Val Pro
 210 215 220

Val Tyr Asp Leu Leu Leu Glu Met Leu Asn Ala His Val Leu Arg Gly
 225 230 235 240

Cys Lys Ser Ser Ile Thr Gly Ser Glu Cys Ser Pro Ala Glu Asp Ser
 245 250 255

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49/57

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Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
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Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
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 Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
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 Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
 65 70 75 80
 Met Phe Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
 85 90 95
 Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
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Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
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Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
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Cys Met Lys Thr Leu Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
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Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
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Lys

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International Bureau



(43) International Publication Date
27 February 2003 (27.02.2003)

PCT

(10) International Publication Number
WO 03/015692 A3

(51) International Patent Classification⁷: **G06F 17/00**

(21) International Application Number: **PCT/US02/22648**

(22) International Filing Date: **17 July 2002 (17.07.2002)**

(25) Filing Language: **English**

(26) Publication Language: **English**

(30) Priority Data:
60/305,902 **17 July 2001 (17.07.2001)** **US**

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(72) Inventors; and

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Huaqiang, Eric [US/US]; C/o Van Andel Research Institute, 333 Bostwick, N.E., Grand Rapids, MI 49503 (US). **DELVES, Christopher, J.** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB).

(74) Agents: **LEVY, David, J. et al.**; GlaxoSmithKline, Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
2 October 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CRYSTALLIZED GLUCOCORTICOID RECEPTOR LIGAND BINDING DOMAIN POLYPEPTIDE AND SCREENING METHODS EMPLOYING SAME

(57) Abstract: A method of modifying a test nuclear receptor (NR) polypeptide is disclosed. The method provides a test NR polypeptide sequence having a characteristic that is targeted for modification; aligning the test NR polypeptide sequence with at least one reference NR polypeptide sequence for which an X-ray structure is available; building a three-dimensional model for the test NR polypeptide using the three-dimensional coordinates of the X-ray structure(s) of at least one reference polypeptide and its sequence alignment with the test NR polypeptide sequence; examining the three-dimensional model of the test NR polypeptide sequence for characteristic differences with the reference polypeptide; and mutating at least one amino acid residue in the test NR polypeptide sequence at a characteristic difference, whereby the test NR polypeptide is modified.

WO 03/015692 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/22648

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G06F 17/00

US CL : 702/27, 19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 702/27, 19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JAGERSCHMIDT et al. Residues in the Ligand Binding Domain That Confer Progestin or Glucocorticoid Specificity and Modulate the Receptor Transactivation Capacity. Molecular Endocrinology. 2000, Volume 14, Number 7, pages 1028-1037, see entire document.	1-5
X	WO 00/52050 A2 (GILLNER et al) 08 September 2000 (08.09.2000), see entire document.	1-5
X	DEY et al. Homology modelling of the ligand-binding domain of glucocorticoid receptor: binding site interactions with cortisol and corticosterone. Protein Engineering. 2001, Volume 14, Number 8, pages 565-571, see entire document.	1-5
X	BLEDSON et al. Crystal Structure of the Glucocorticoid Receptor Ligand Binding Domain Reveals a Novel Mode of Receptor Dimerization and Coactivator Recognition. Cell. 12 July 2002, Volume 110, pages 93-105, see entire document.	1-5

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

12 June 2003 (12.06.2003)

Date of mailing of the international search report

27 JUN 2003

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703)305-3230

Authorized officer

Channing S. Mahatan

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/22648

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claim Nos.: 19-22 and 24-27
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-5

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-5, drawn to a method of modifying a test NR polypeptide.

Group II, claim(s) 6-12, drawn to a method of modifying a test NR polypeptide.

Group III, claim(s) 13-18, drawn to a GR polypeptide.

Group IV, claim(s) 23, drawn to a method of detecting a nucleic acid molecule encoding a GR polypeptide.

Group V, claim(s) 28-47, drawn to a GR ligand binding domain polypeptide crystal.

Group VI, claim(s) 48-59, drawn to a method for determining the three-dimensional structure of a crystallized GR ligand binding domain polypeptide.

Group VII, claim(s) 60-68, drawn to a method of generating a crystallized GR ligand binding domain polypeptide.

Group VIII, claim(s) 69-77, drawn to a method of designing a modulator of a nuclear receptor.

Group IX, claim(s) 78-89, drawn to a method of designing a modulator of GR-alpha polypeptide.

Group X, claim(s) 90-92, drawn to a method of screening for a modulator of a GR ligand binding domain polypeptide.

Group XI, claim(s) 93-95 and 96-98, drawn to a method for identifying a GR modulator.

Group XII, claim(s) 99-109, drawn to a method of designing a modulator of a GR polypeptide.

Group XIII, claim(s) 110-113, drawn to a method for identifying a compound that inhibits binding of a ligand to a GR polypeptide.

Group XIV, claim(s) 114-116, drawn to a method of identifying a NR modulator.

The inventions listed as Groups I-XIV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group I is considered to be the sequence having a characteristic that is targeted for modification.

The special technical feature of Group II is considered to be the sequence having a solubility, stability in solution, other solution behavior, tendency to fold properly, ability to form ordered crystals different from that desired.

The special technical feature of Group III is considered to be GR polypeptide.

The special technical feature of Group IV is considered to be detection of the duplex structure.

The special technical feature of Group V is considered to be the crystal.

The special technical feature of Group VI is considered to be a resolution of about 2.8 Angstroms or better.

The special technical feature of Group VII is considered to be the hanging drop method.

The special technical feature of Group VIII is considered to be the step of designing a modulator of a nuclear receptor.

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The special technical feature of Group IX is considered to be synthesizing a modulator based on the three-dimensional structure of the crystalline of the GR alpha ligand binding domain polypeptide.

The special technical feature of Group X is considered to be detection of interaction.

The special technical feature of Group XI is considered to be conformationally constrained residues.

The special technical feature of Group XII is considered to be the step of comparing the biological activity of the GR polypeptide in the presence and absence of a modified ligand.

The special technical feature of Group XIII is considered to be the step of determining an amount of ligand bound to the GR polypeptide.

The special technical feature of Group XIV is considered to be comparison of atomic structure coordinate sets.

Groups I, II, IV, and VI-XIV are drawn to methods having different goals, method steps, and starting materials which do not share the same or a corresponding special technical feature. Groups III and V are drawn to structurally different products which do not share the same or a corresponding technical feature. Note PCT Rule 13 does not provide for multiple products or methods within a single application.

Thus, in summary the inventions listed as Groups I-XIV are not linked as to form a single general inventive concept ("requirement of unity of invention").

Continuation of B. FIELDS SEARCHED Item 3:

US PAT FULL, MEDLINE, BIOSIS, CAPLUS, BIOTECHDS, EMBASE

search terms: nuclear receptor, glucocorticoid, progesterone, ligand binding domain, X-ray, coordinate, modeling, three-dimensional